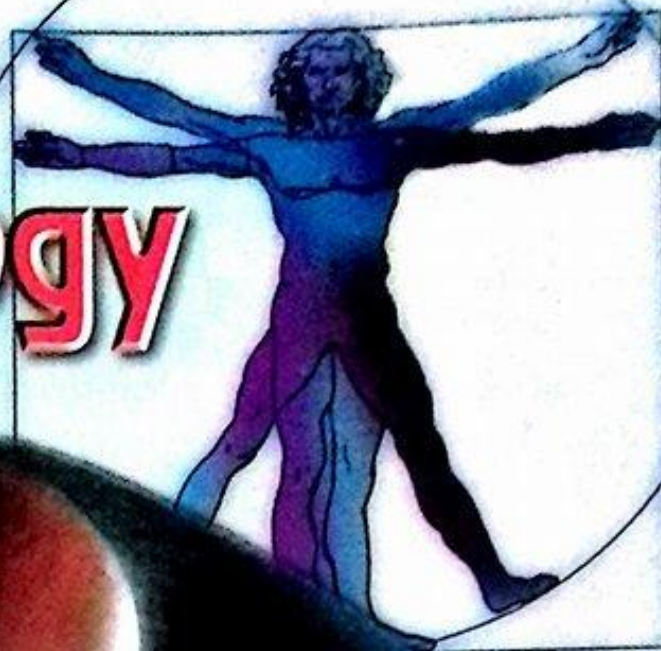


Special Embryology



scanned by

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Prof. Dr.

Ahmed M. Kamal

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Foregut → cranial part & caudal part.

PHARYNGEAL (BRANCHIAL) APPARATUS & HEAD AND NECK**Introduction**

After folding, the 2ndry yolk sac inside the embryo will form the fore, mid, and hindgut (details of the gut will be discussed with the digestive system).

The foregut is divided into: i. Cranial part & ii. Caudal part.

The cranial part extends from the oral membrane to the laryngotracheal groove. This part gives rise to part of the mouth cavity, salivary glands, pharyngeal apparatus and respiratory system.

The caudal part begins distal to the laryngotracheal groove and continues with the midgut at the hepatic bud. This part gives rise to esophagus, stomach, part of the duodenum, liver, biliary system and pancreas (details will be discussed with the digestive system).

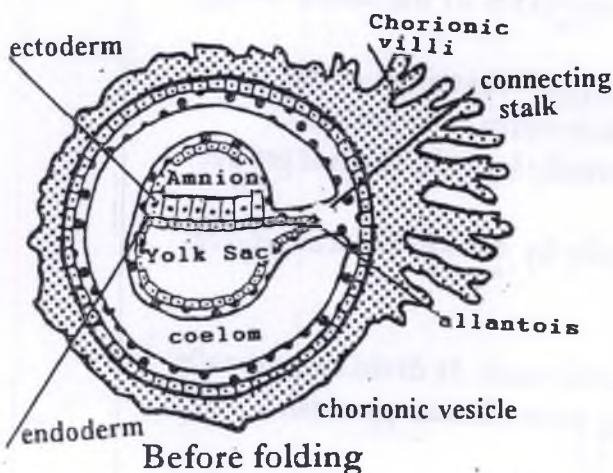
The pharyngeal apparatus contributes greatly to the formation of head and neck.

It consists of: A. Pharyngeal arches. B. Pharyngeal pouches.

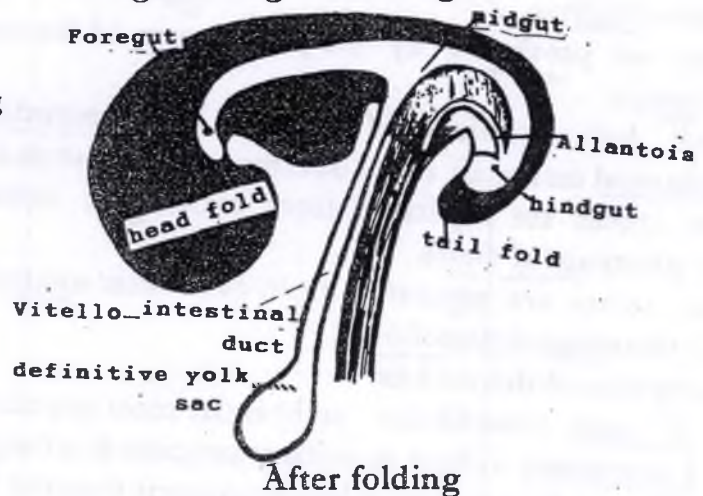
C. Pharyngeal clefts. D. Pharyngeal membranes.

Summary & Illustrations**Introduction**

After folding, the secondary yolk sac → Foregut, midgut & hindgut



Before folding



After folding

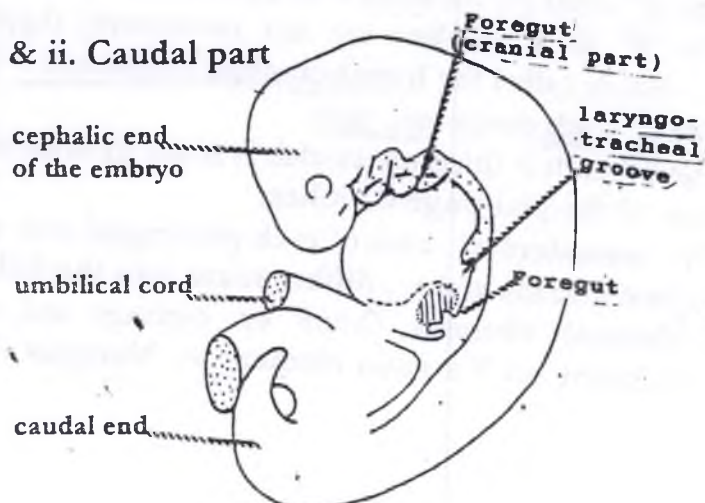
Foregut is divided into: i. Cranial part & ii. Caudal part

i. Cranial part gives:

part of mouth, salivary glands, pharyngeal apparatus, & respiratory system

ii. Caudal part (distal to laryngo-

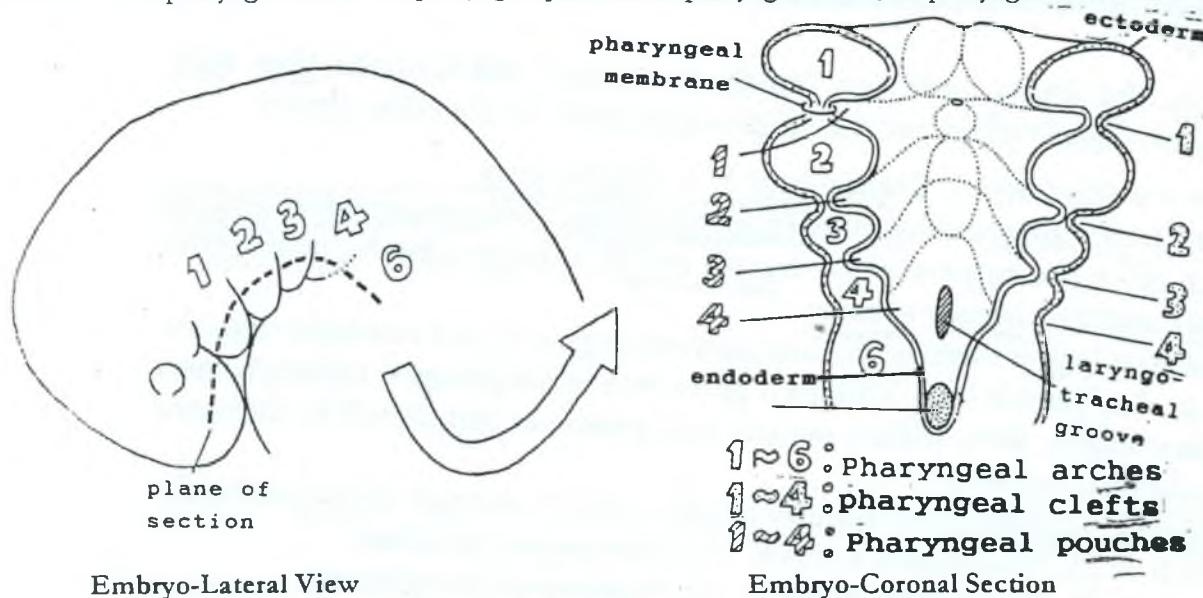
tracheal groove) gives: esophagus, stomach, part of duodenum, liver & biliary system & pancreas.



Summary & Illustrations

Pharyngeal apparatus

Consists of: A. pharyngeal arches, B. pharyngeal pouches, C. pharyngeal clefts, D. pharyngeal membranes.



Embryo-Lateral View

Embryo-Coronal Section

A. Pharyngeal arches

They are 6 curved cylindrical **mesodermal thickenings** on each side of the primitive **pharynx**.

They are **produced** by the proliferation of the **mesoderm** of the lateral wall of the **pharynx**.

Each arch consists of : i) an **outer ectodermal** covering, ii) an **inner endodermal** lining, iii) a **mesodermal core** between ectoderm & endoderm.

The arches are separated from each other externally by **ectodermal** grooves called **pharyngeal clefts**.

The arches are separated from each other internally by 4 **endodermal** grooves called **pharyngeal pouches**.

Description of the arches:

The **1st arch** (**mandibular arch**) is the most prominent arch. It divides externally into 2 **processes**: a short **maxillary process** & a long **mandibular process**.

The **2nd arch** (**hyoid arch**) is less prominent than the 1st.

The **3rd & 4th arches** are not prominent, their ventral ends meet in a median swelling called the **hypobranchial eminence**.

The **5th arch** disappears early.

The **6th arch** is the most caudal. It is not prominent on the surface.

Fate of the pharyngeal arches:

The **mesodermal core** of each pharyngeal arch and the **neural crest cells** (which migrate into the arches) **differentiate** into the following **derivatives**:

- i. **Skeletal element** (bone or cartilage and connective tissue),
- ii. **Muscular element**,
- iii. **Vascular element**,
- iv. **Nervous element**.

Derivatives of the pharyngeal arches

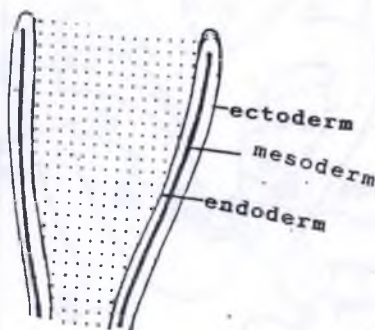
Arch	Skeletal element (from neural crest cells)	Muscular element	Vascular element (aortic arches)	Nervous element
First (mandibular) arch	Malleus Incus. Spine of sphenoid Sphenomandibular ligament Lingula & Meckel's cartilage of the mandible.	Muscles of mastication. Tensor palati Tensor tympani. Mylohyoid. Ant. belly of digastric.	Maxillary a.	Mandibular n. (V)
Second (hyoid arch)	Stapes. Styloid process. Stylohyoid ligament Lesser cornu and upper part of body of hyoid bone.	Muscles of face. Platysma. Post. belly of digastric. Stylohyoid. Stapedius.	Artery to stapedius	Facial n. (VII)
Third	Greater cornu and lower part of body of hyoid bone.	Stylopharyngeus	Internal and common carotid as.	Glossopharyngeal n. (IX)
Fourth	Thyroid cartilage	Cricothyroid	Aortic arch on left side . Subclavian a. on right side .	Superior laryngeal n. (X)
Sixth	Other cartilages of larynx (cricoid, arytenoid, corniculate, & cuneiform)	Other intrinsic muscles of the larynx + Constrictor muscles of pharynx + Muscles of palate except tensor palati.	Pulmonary arteries (one on each side). Ductus arteriosus on left side .	Recurrent laryngeal n. (X)

Summary & Illustrations

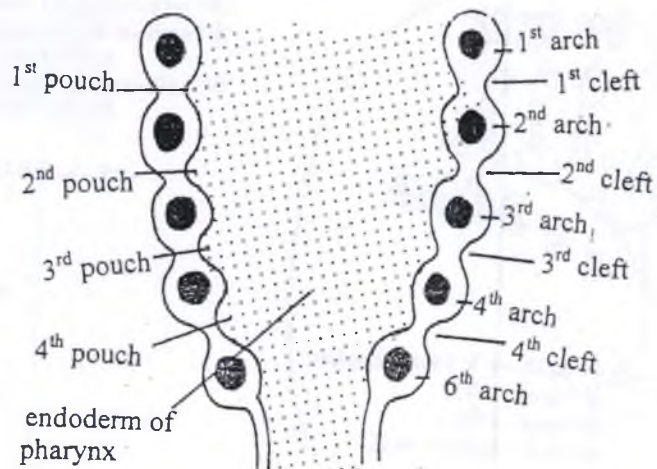
A. Pharyngeal arches

Produced by **proliferation of the mesoderm** of the lateral wall of the pharynx.

The arches are separated from each other externally by ectodermal **clefts** and internally by endodermal **pouches**.



The wall of the pharynx at an early stage
(coronal section)



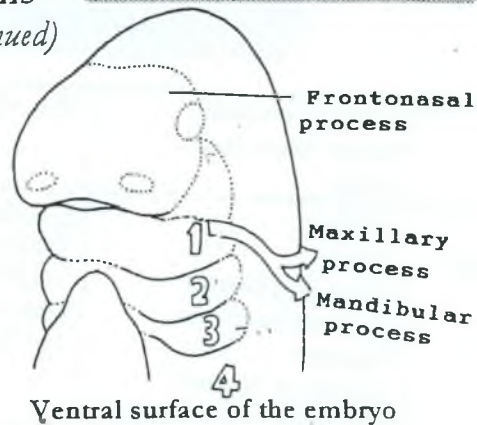
The wall of the pharynx after development
of the arches (coronal section)

Summary & Illustrations

Pharyngeal arches (continued)

Description of the arches:

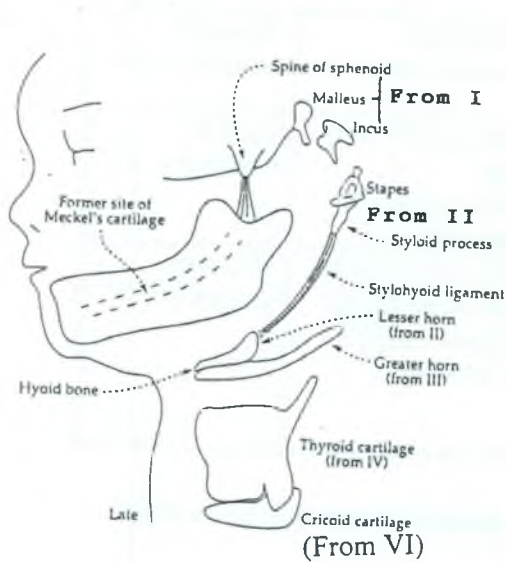
- The 1st divides into maxillary and mandibular processes
- The 2nd is less prominent
- The 3rd and 4th are not prominent & meet ventrally in the hypobranchial eminence
- The 5th disappears
- The 6th is not prominent on the surface



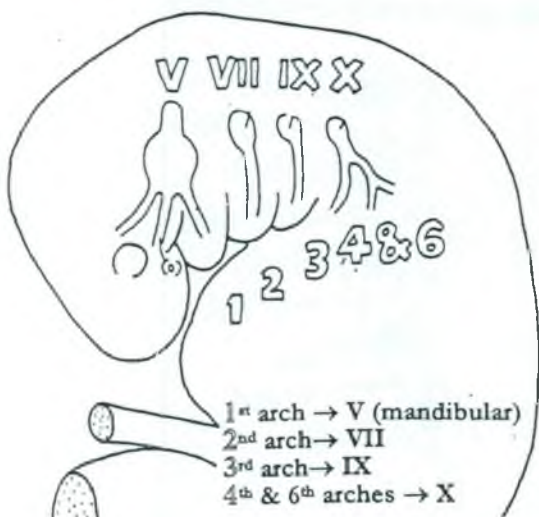
Derivatives of the pharyngeal arches

Each arch differentiates into:

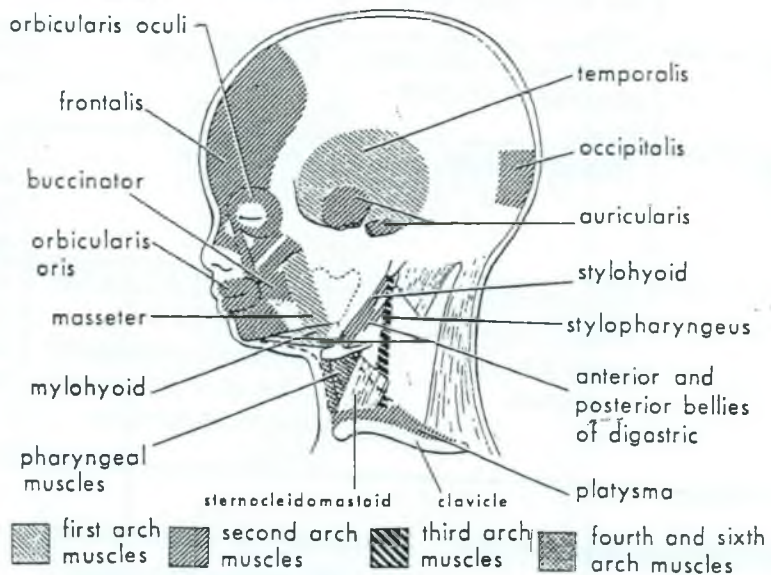
- i. Skeletal element
- ii. Muscular element
- iii. Vascular element
- iv. Nervous element



i. Skeletal element

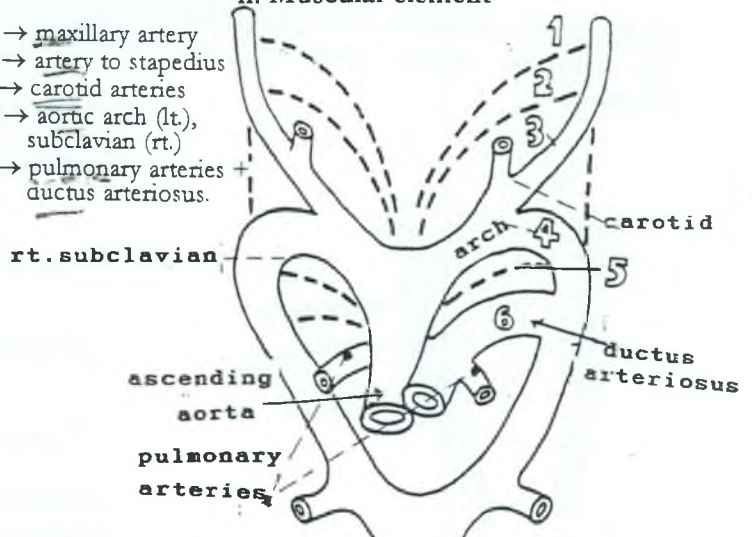


iii. Nervous element



ii. Muscular element

- 1st arch → maxillary artery
- 2nd arch → artery to stapedius
- 3rd arch → carotid arteries
- 4th arch → aortic arch (lt.), subclavian (rt.)
- 6th arch → pulmonary arteries + ductus arteriosus.



iv. Vascular element

B: Pharyngeal pouches

There are **5 pairs** of pharyngeal pouches. The last one of these is often considered as part of the **4th**. The endodermal lining of these pouches gives rise to:

1st Pouch:

It gives rise to the **tubotympanic recess** which forms:

- a) **Tympanic** (middle ear) cavity.
- b) **Pharyngo-tympanic** (auditory) tube.

2nd Pouch:

It gives rise to the **palatine tonsil**

3rd Pouch:

It gives rise to:

- a) **Thymus gland** (migrates caudally to enter the chest).
- b) **Inferior parathyroid glands**.

4th Pouch:

It gives rise to:

- a) **Superior parathyroid glands**.
- b) A **small part of thyroid gland** (most of the thyroid comes from the thyroglossal duct).

5th Pouch:

This pouch is usually considered to be a part of the 4th pouch.

It gives rise to the **ultimobranchial body** which is later incorporated in the **thyroid gland**. The ultimobranchial body gives the **parafollicular (C) cells** which secrete **calcitonin** hormone.

Development of the thymus gland:

It is developed from the **3rd** pouch. Each lobe (one from each side) grows downwards into the thorax. The lobes lose their connection from the pharyngeal wall and lie close together in front of the pericardium and great vessels.

Changes with age:

The thymus is well developed during fetal life, reaches its maximum in the **2nd** year. After birth, the size of the gland remains constant till puberty, when the gland starts to degenerate gradually.

Development of the parathyroid glands:

The **superior parathyroid glands** are developed from the endoderm of the **4th** pharyngeal pouch.

The **inferior parathyroid glands** are developed from the endoderm of the **3rd** pharyngeal pouch.

The **inferior parathyroid glands** (from **3rd** pouch) descend to a lower level than the **superior parathyroids** (from **4th** pouch) due to connection of the inferior glands to the thymus with which they migrate caudally).

Development of the palatine tonsil:

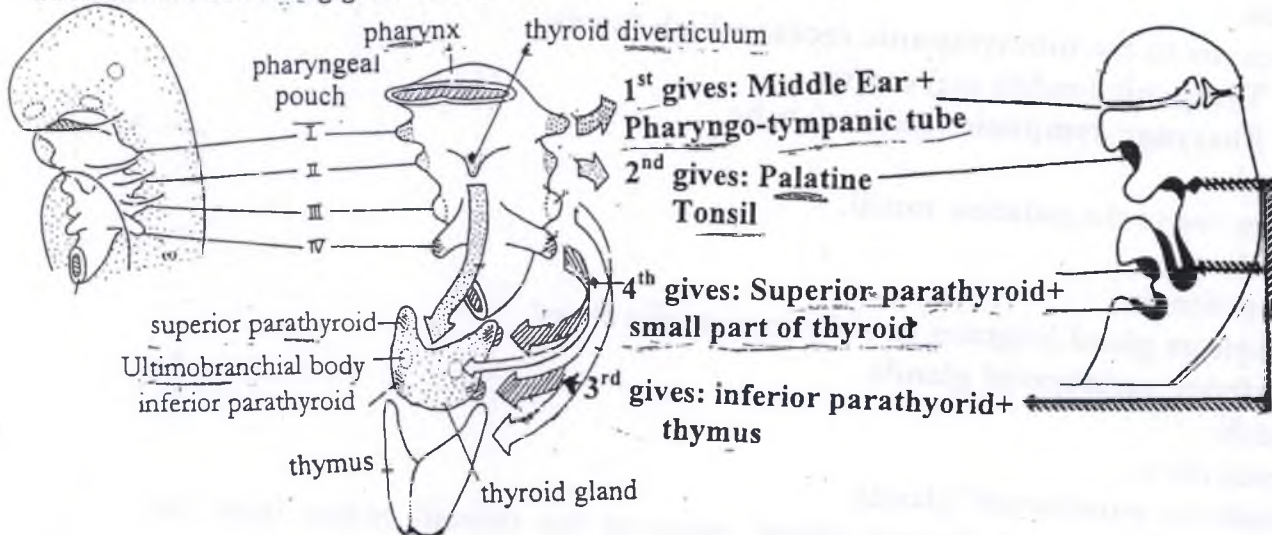
It arises from the endoderm of the dorsal part of the **2nd** pouch as follows:

- i. The endoderm proliferates to form a group of **buds**.
- ii. The buds become canalized to form **crypts**.
- iii. **Lymphocytes** (mesodermal in origin) then invade the tonsillar tissue.
- iv. The remnant of the cavity of the second pouch forms the inter-tonsillar cleft.

Summary & Illustrations

B. Pharyngeal Pouches

There are 5 pairs of pouches. The 5th is not marked and is considered as part of the 4th.
Their endodermal lining gives rise to :

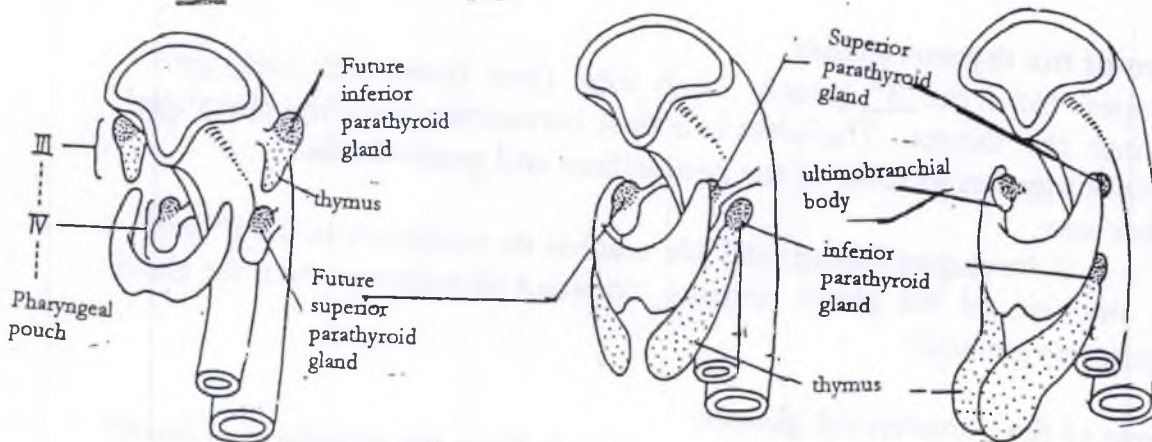


Development of the thymus & parathyroid glands

The thymus is developed from the 3rd pouch and migrates downward into the thorax dragging with it the inferior parathyroid.

The superior parathyroid are developed from the endoderm of the 4th pouch.

The inferior parathyroid develop from the 3rd pouch and descend to a lower level than the superior parathyroid dragged by the migrating thymus.



Week 6- inferior parathyroid + thymus are higher than the superior parathyroid

Week 8- inferior parathyroid + thymus are lower than the superior parathyroid

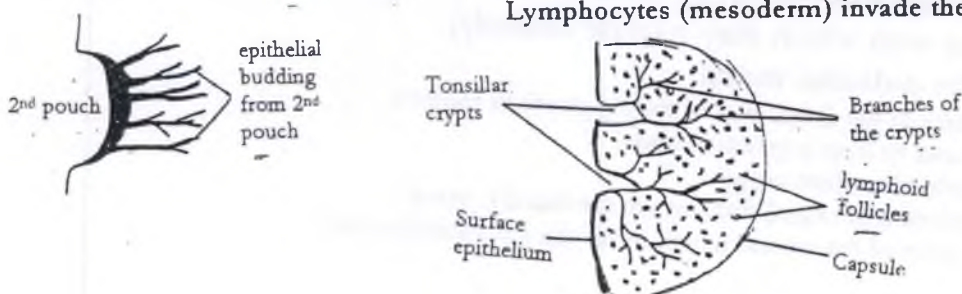
Week 10- The 2 lobes of thymus unite & migrate to the thorax

Development of palatine tonsil

It arises from endoderm of 2nd pouch

The buds canalize → crypts.

Lymphocytes (mesoderm) invade the tonsillar tissue.



1st → external auditory meatus.

C. Pharyngeal clefts

There are 4 pairs of pharyngeal clefts, their ectodermal lining gives rise to:

1st cleft gives rise to the external auditory meatus.

2nd, 3rd, and 4th clefts form the floor of a depression termed the cervical sinus which is open ventrally.

The sinus becomes gradually reduced in size and is finally obliterated by approximation of its walls.

D. Pharyngeal membranes

1st membrane gives rise to the tympanic membrane, which consists of surface ectoderm of the 1st cleft, and the endoderm of the 1st pouch. The other membranes form no definite adult structures.

Anomalies of the pharyngeal apparatus

1. Pharyngeal (Branchial) cyst:

It is developed from a remnant of the cervical sinus.

2. Pharyngeal (Branchial) fistula:

The cervical sinus may persist and opens by a long duct, as follows:

It may open on the external surface of the neck (just close to the anterior border of sternomastoid).

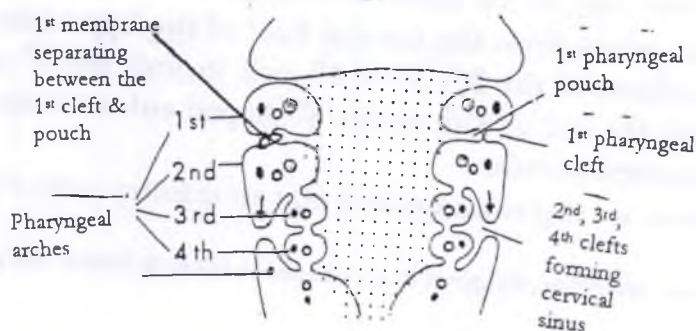
It may open into the pharynx close to the tonsil (2nd pouch).

Summary & Illustrations

C: Pharyngeal clefts

1st cleft → external auditory meatus

2nd, 3rd, & 4th clefts → cervical sinus → finally obliterated.

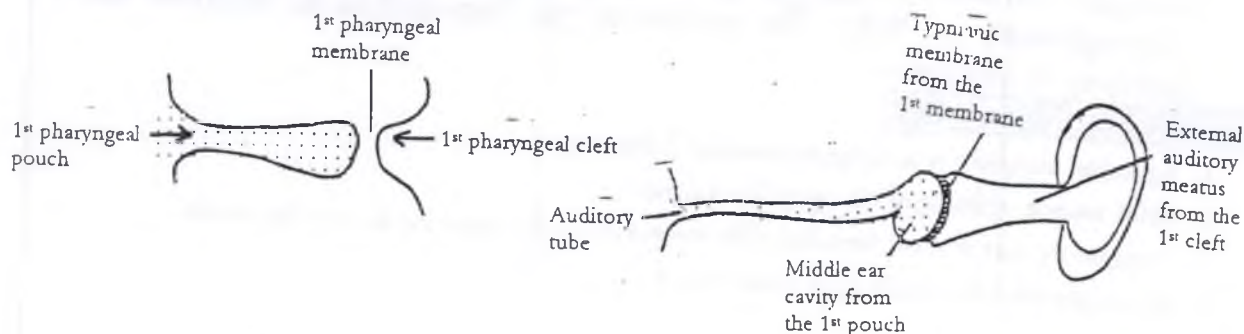


D. Pharyngeal membranes

Only, the 1st membrane persists, separating between:

1st pouch which gives tympanic cavity + auditory tube & 1st cleft which gives ext. auditory meatus.

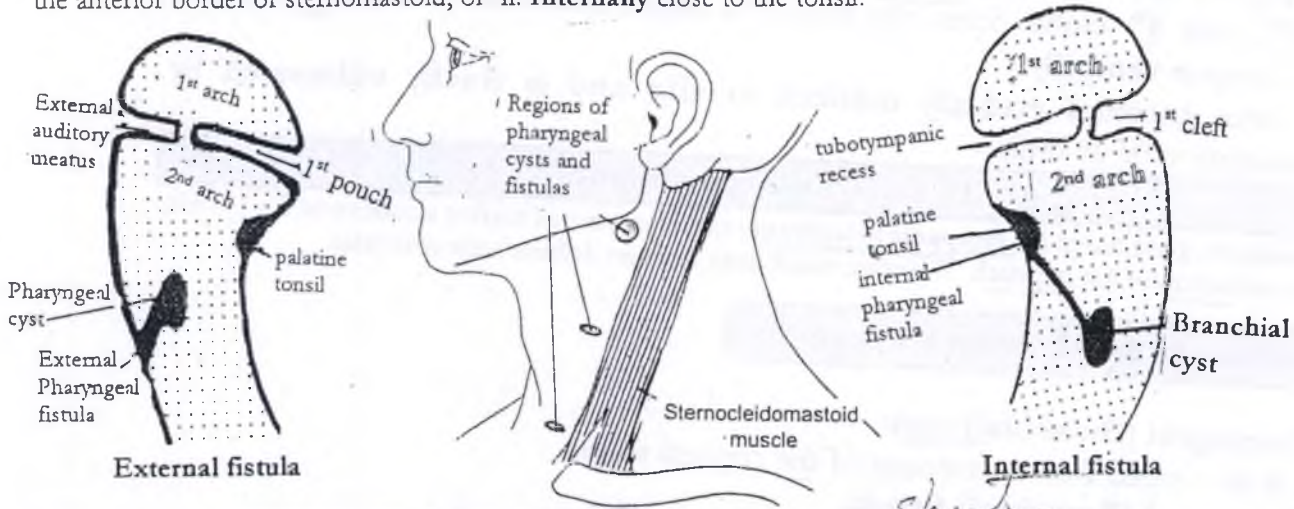
The 1st membrane gives the tympanic membrane.



Summary & Illustrations

Anomalies of the pharyngeal apparatus

1. **Pharyngeal (Branchial) cyst**: non obliteration of a part of cervical sinus
2. **Pharyngeal (Branchial) fistula**: persistence of the cervical sinus which may open: i. **Externally**; on the anterior border of sternomastoid, or ii. **Internally** close to the tonsil.



Development of the tongue

The tongue develops from several parts:

The mucous membrane:

A. Anterior 2/3: arise from 3 swellings derived from the endoderm of the 1st pharyngeal arch:

1. **tuberculum impar**: small median elevation between the ventral ends of the 1st pharyngeal arch.
2. **lingual swellings**: on either side of the tuberculum impar.

B Posterior 1/3 of tongue: arises from the cranial half of the hypo branchial eminence i.e. from the endoderm of the 2nd, 3rd & 4th arch (mainly the 3rd arch).

The posterior 1/3 fuses with the ant. 2/3 along the V-shaped **sulcus terminalis**, the apex of the V is called **foramen cecum**.

N.B.: The **hypobranchial eminence**, is a large swelling derived from the endoderm of the 2nd, 3rd and 4th pharyngeal arch.

- The **cranial part** (mainly from the 3rd arch) grows in a v-shaped manner & forms the posterior 1/3 of the tongue.
- The **caudal part** (mainly from the 4th arch) forms the **epiglottis**.

Muscles of the tongue:

- Derived from **3 occipital myotomes** which migrate ventrally to reach the mucous membrane of the tongue **dragging with them their nerve supply** (hypoglossal n. XII). The course of the hypoglossal n. indicates the pathway of migration.

Anomalies of the tongue:

1. **Aglossia**: complete or incomplete absence of the tongue.
2. **Bifid tongue**: splitting of the tip of the tongue.
3. **Tongue-tie**: due to short frenulum. The tongue is not free from the floor of the mouth.
4. **Macroglossia**: abnormally large-sized tongue.

- Lingual Thyroid Retrosternal goiter

- Thyroid agenesis - thyroglossal cyst - thyroglossal fistula *Special Embryology 10*

Correlation between the development of the tongue and its nerve supply:

- The mucous membrane of the anterior 2/3 is derived from the endoderm of the 1st arch. So it is supplied by the mandibular division of trigeminal nerve (V) which is the nerve supply of the first arch.
- The mucous membrane of the posterior 1/3 is derived from the endoderm of the 3rd arch. So it is supplied by the glossopharyngeal nerve (IX) which is the nerve supply of the 3rd arch.

The muscles of the tongue are derived from the occipital myotomes so they are supplied by the hypoglossal nerve (XII).

Development of Thyroid Gland

The **Thyroid gland** appears at the 4th week as **endodermal thickening** in the **floor of pharynx** between the **tuberculum impar** & the **hypobranchial eminence** (at the site indicated by the **foramen cecum** in the adult tongue).

This thickening is evaginated to form a **bilobed thyroid diverticulum** which descends downward in the neck in front of hyoid bone & laryngeal cartilages.

Its distal end is enlarged to form the thyroid gland.

The proximal part forms a duct called **thyroglossal duct**, (because the tongue develops around the upper end of this duct).

The thyroid gland finally reaches its position in front of the thyroid cartilage & upper part of trachea.

The thyroglossal duct becomes obliterated & disappears (or fibrosed to form the **levator glandulae thyroidae**).

Anomalies:

1. **Thyroid agenesis**: congenital absence of thyroid gland leading to cretinism.
2. **Lingual thyroid**: the thyroid fails to descend & lies in the substance of the tongue.
3. **Thyroglossal cyst**: due to persistence of a part of the thyroglossal duct unobliterated (any where along the line of descent of the thyroid gland).
4. **Thyroglossal fistula**: When the cyst forms a canal open onto the skin.
5. **Retrosternal goiter**: The thyroid may descend more to reach the thorax.

Summary & Illustrations

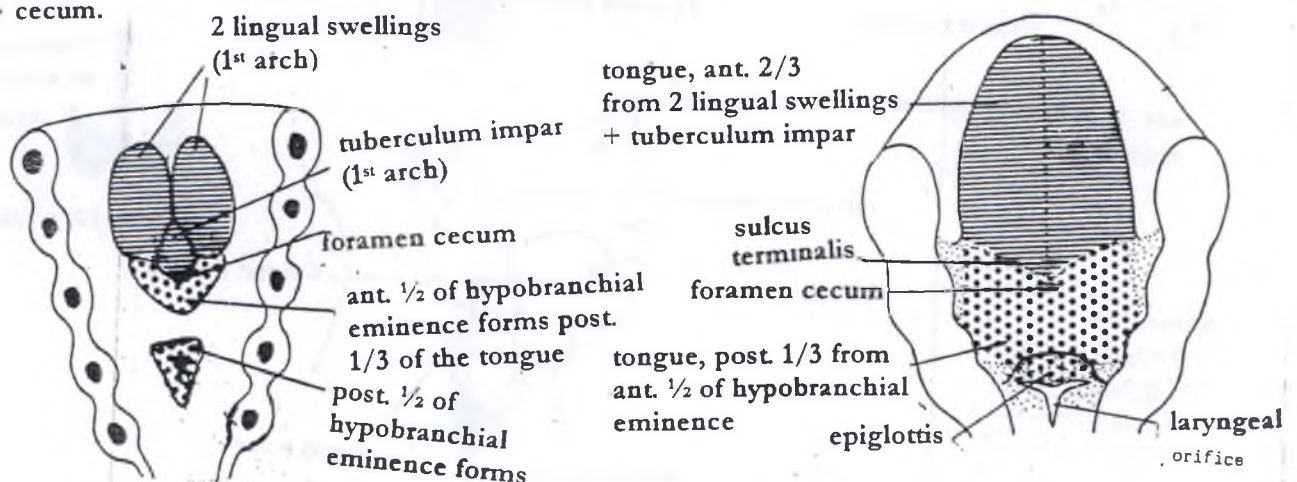
Development of the tongue

1. The mucous membrane:

a. **Anterior 2/3** from 2 **lingual swellings** and **tuberculum impar** (from 1st arch) supplied by mandibular (V) nerve.

b. **Posterior 1/3** from **anterior 1/2 of hypobranchial eminence** (from 3rd arch) supplied by IX nerve.

V-shaped **sulcus terminalis** forms the line of fusion between the 2 parts. Its apex is called **foramen cecum**.

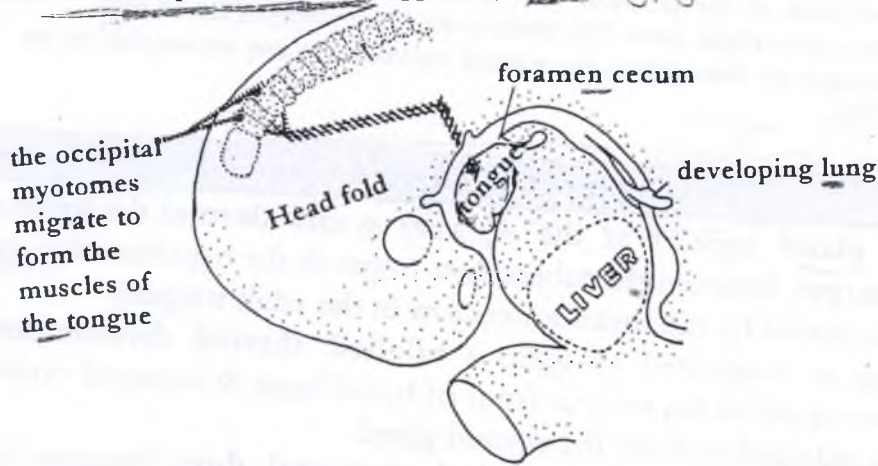


Anomalies - Bifid Tongue - Tongue tie macroglossia

Summary & Illustrations

Development of the tongue (continued)

2. The muscles arise from occipital myotomes supplied by XII n. *hypoglossal.*

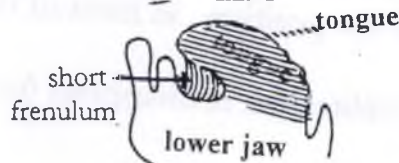


Anomalies:

1. Bifid tongue



2. Tongue tie (with short frenulum)



3. Macroglossia (large tongue)



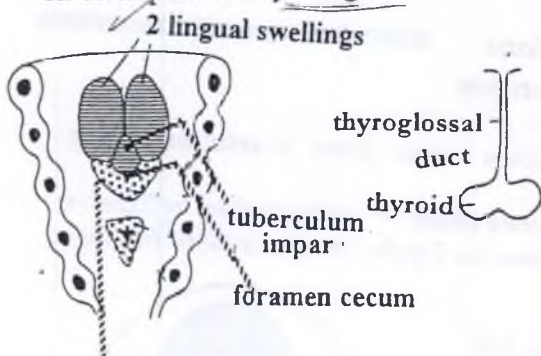
Development of the thyroid gland

-From the endoderm of the thyroid diverticulum

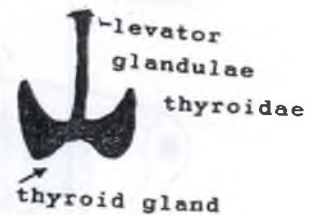
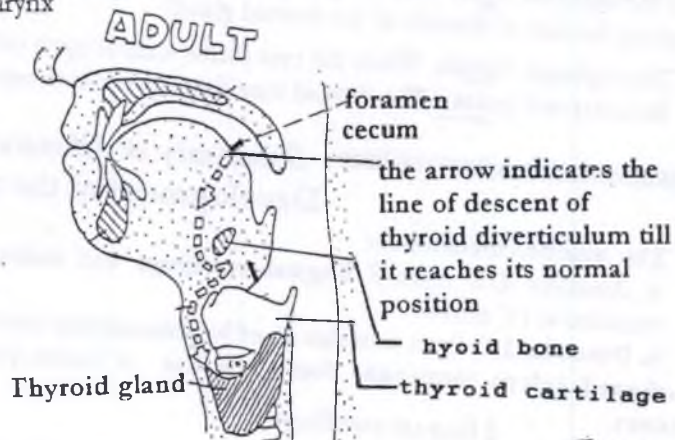
-The diverticulum arises from the foramen coecum between the tuberculum impar and the hypobranchial eminence in the floor of the pharynx

-Its proximal part → thyroglossal duct

-Its distal part → Thyroid gland

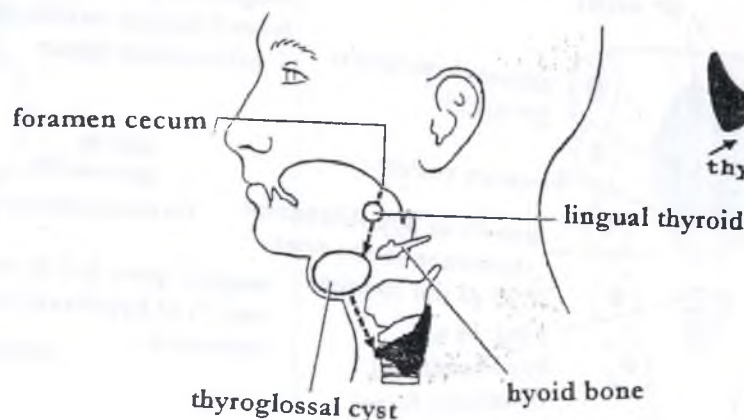


ant. 1/2 of hypobranchial eminence



Anomalies

1. Lingual thyroid
2. Thyroglossal cyst
3. Thyroglossal sinus
4. Retrosternal goiter

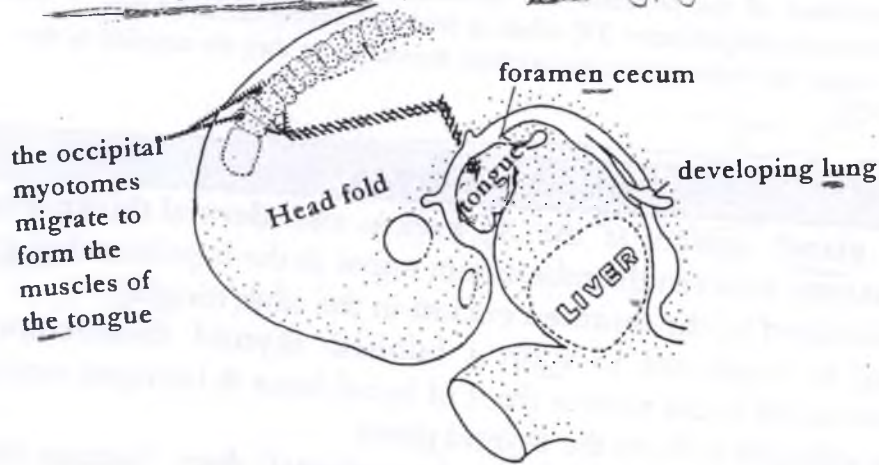


Anomalies - Bifid Tongue - Tongue tie - Macroglossia

Summary & Illustrations

Development of the tongue (continued)

2. The muscles arise from occipital myotomes supplied by XII n. *hypoglossal.*

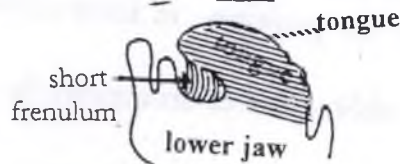


Anomalies:

1. Bifid tongue



2. Tongue tie (with short frenulum)



3. Macroglossia (large tongue)



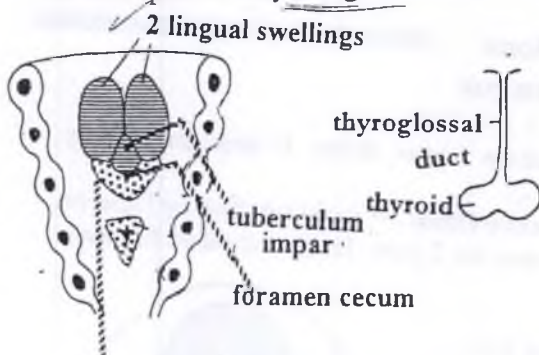
Development of the thyroid gland

-From the endoderm of the thyroid diverticulum

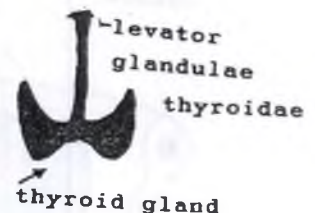
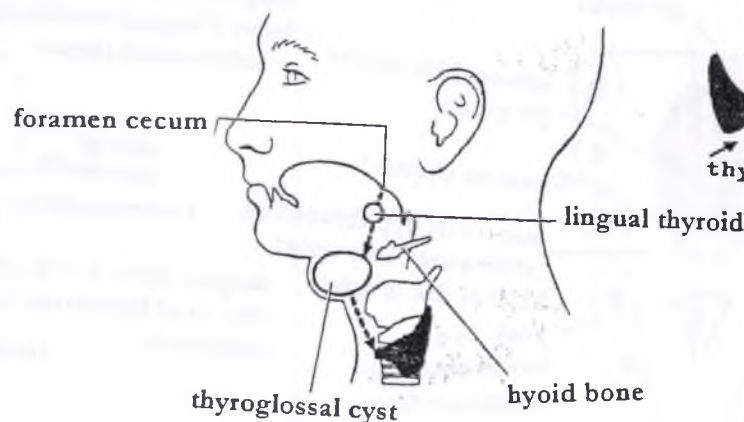
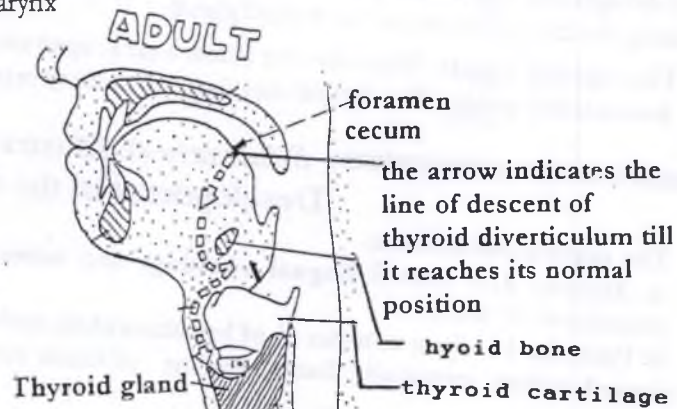
-The diverticulum arises from the foramen coecum between the tuberculum impar and the hypobranchial eminence in the floor of the pharynx

-Its proximal part → thyroglossal duct

-Its distal part → Thyroid gland



ant. 1/2 of hypobranchial eminence



Anomalies

1. Lingual thyroid
2. Thyroglossal cyst
3. Thyroglossal sinus
4. Retrosternal goiter

Development of the Face

The upper part of the head fold enlarges to form **frontonasal process**.

On either of this process lies the 1st pharyngeal arch.

The 1st arch gives rise to two processes

- i- Mandibular process above. ii- Maxillary process below

Ventrally the frontonasal process + 2 processes of the 1st arch encircle the future mouth of the embryo (stomodeum).

- Forehead and nose are formed from the **fronto-nasal process**.
- Cheeks are formed by the fused lateral parts of **maxillary and mandibular processes**.
- Upper lip is formed by **maxillary processes on either side + inter maxillary segment (premaxilla)** of the frontonasal process in the middle (which will form the philtrum of the upper lip).
- Lower lip is formed by the fusion of the 2 mandibular processes.

Each maxillary process grows medially and approaches the frontonasal process and the premaxilla.

At the line of fusion between the frontonasal process and maxillary process, the nasolacrimal duct is formed.

- Muscles of the face develop from the second arch.

Development of the Nose

- An epithelial thickening is formed on each side of the fronto-nasal process. This is called **olfactory placode**.
- The placode is depressed to form the **olfactory pit**. The pit is bounded medially by the **medial nasal process** and laterally by the **lateral nasal process**. The lateral process grows medially towards the medial process, thus converting the pit into the **primitive nasal cavity**.
- The cavity gets deeper and opens into the primitive mouth.
- Two horizontal palatine processes are developed from the maxillary processes.

They fuse together in the median plane to form the **main part of the palate** (2ry palate), which will separate the nasal cavity from the mouth cavity.

- At the same time, the **frontonasal process becomes thinner to form the nasal septum**. It fuses with the palate to divide the nasal cavity into two halves.

Projections appear in the lateral wall to form the Conchae.

Diverticula from the lateral wall form the nasal air sinuses.

Summary of the structures contributing to formation of the face and nose

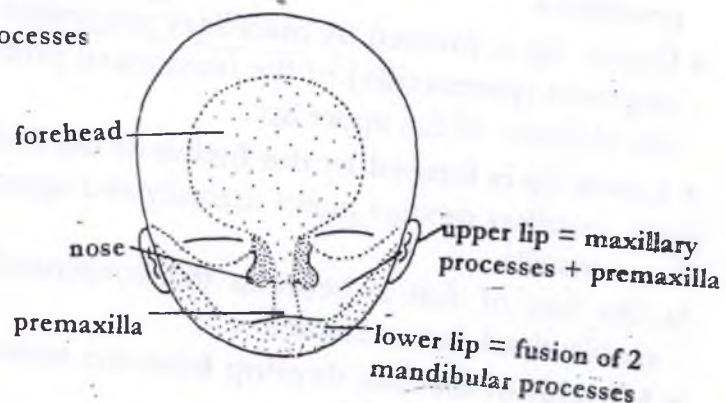
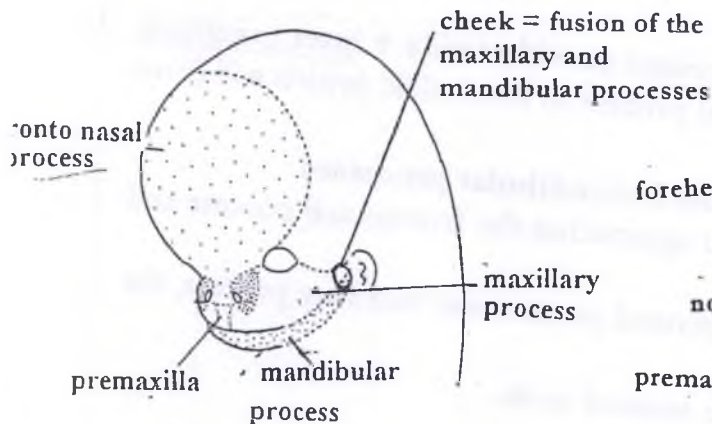
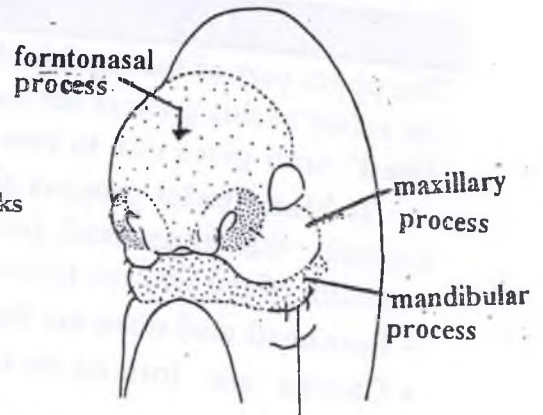
Process	Structures formed
Frontonasal	Forehead, bridge and septum of the nose, premaxilla of upper lip + med & lat. nasal processes.
Medial nasal	Nasal crest + tip of the nose
Lateral nasal	Ala of the nose
Maxillary	Lateral part of the upper lip + cheeks
Mandibular	Lower lip

Summary & Illustrations Development of the face

The face is developed from:

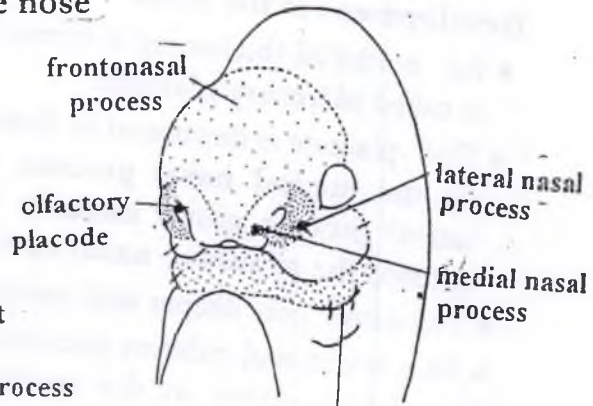
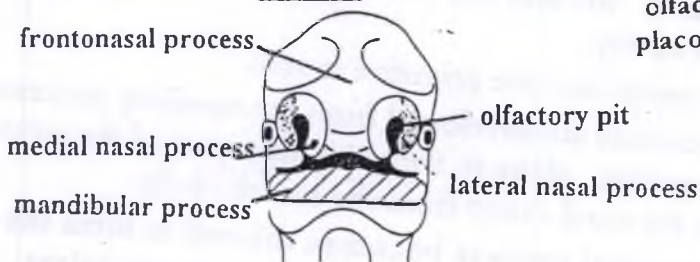
- i. Frontonasal process (upper part of head fold)
- ii. The 2 processes (maxillary and mandibular of the 1st arch)

- The frontonasal process → **Forehead + nose**
- Fusion of the lateral part of the maxillary & mandibular process → **cheeks**
- The upper lip** = maxillary processes on either side + premaxilla (part of the frontonasal process)
- The lower lip** = fusion of the 2 mandibular processes

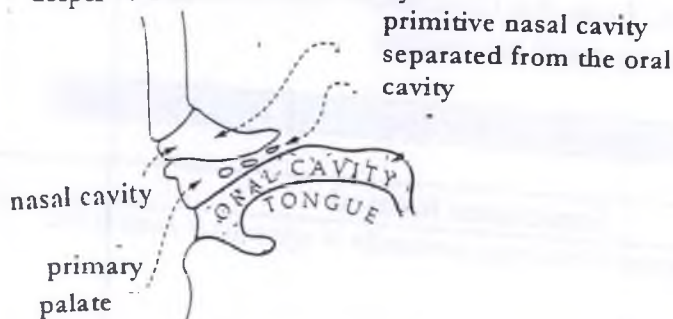


Development of the nose

- Starts as 2 epithelial thickenings (olfactory placodes) on the frontonasal processes
- The placode is surrounded by medial and lateral olfactory processes.
- The placode depressed → **olfactory pit**

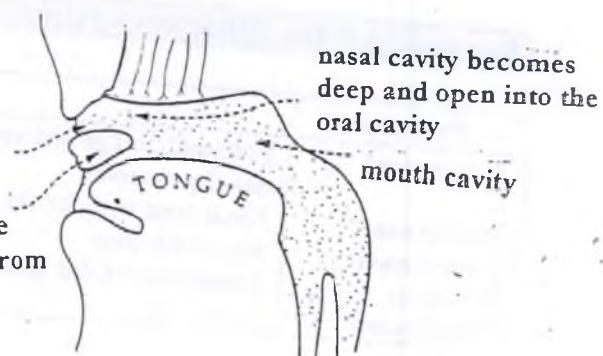


- The olfactory pit becomes deeper → **Primitive nasal cavity**



- The nasal cavity becomes deeper & continues with the mouth cavity

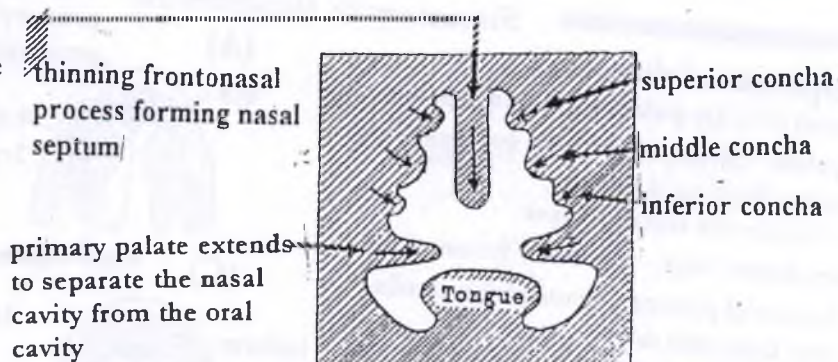
developing palate separates nasal from mouth cavity



Summary & Illustrations

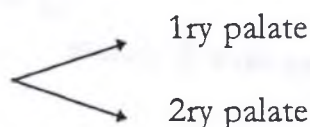
Development of the nose (continued)

- The palate is developed to separate the nasal cavity from mouth cavity
- The frontonasal process becomes thin forming nasal septum



Development of the Palate:

The palate is formed of 2 components



1. The 1ry palate

It is the small triangular part of the palate which carries the incisive fossa.

It develops from the inter maxillary segment (**premaxilla**) of the frontonasal process

2. The 2ndry palate:

It is the remaining large part of the palate.

It is formed by the **horizontal palatine processes of the maxilla** which extend medially from the medial aspect of each maxillary process to fuse. With each other in the middle line. With the 1ry palate anteriorly in a V shaped manner.

The nasal septum descends vertically downwards from the frontonasal process to fuse with the upper surface of the palate in the middle line.

The anterior part of the palate ossifies forming the bony hard palate.

The posterior part of the palate remains fleshy & forms the soft palate.

Congenital anomalies of the face and palate

- 1- **Inclusion dermoid**: Cystic swelling along the lines of fusion of the processes which will form the face
- 2- **Macrostoma** (large mouth): When fusion of the maxillary and mandibular processes occurs in the lateral part of the face.
- 3 **Microstoma** (Small mouth): When the fusion of the maxillary and mandibular processes occur in the medial part of the face.
- 4- **Oblique facial cleft**: It is due to failure of fusion between the maxillary and frontonasal processes.
- 5- **Hare lip** (unilateral cleft lip): It is due to failure of fusion between the maxillary process and the premaxilla (intermaxillary segment of the fronto nasal process). It may occur on one side (unilateral cleft lip) or on both sides (bilateral).
- 6- **Cleft palate**: It is due to failure of fusion between the different segments of plate. - It may be;
 - i- **Unilateral complete cleft palate**: due to failure of fusion between the pre-maxilla and the horizontal palatine process of the maxilla.
 - ii- **Bilateral complete cleft palate**: When the 2 palatine processes fail to fuse with the 1ry palate.
 - iii- **Isolated cleft palate**: It is due to defect in the midline of the palate behind the incisive fossa.
 - iv. **Bifid soft palate** or **bifid uvula** occurs when the 2 palatine processes fail to fuse together in the median plane, only in their most posterior parts.

Summary & Illustrations

Development of the palate

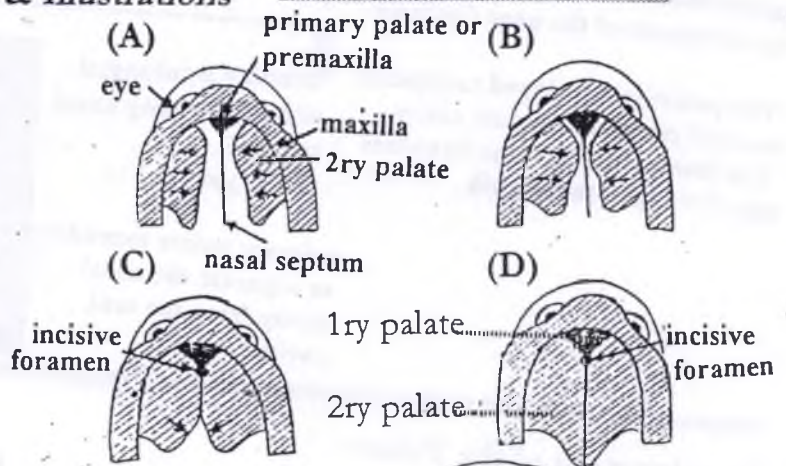
It is formed of i.) 1ry palate & ii.) 2ndry palate

i. **1ry palate**: -developed from the premaxilla of the frontonasal process.

-It carries the incisive fossa

ii. **2ndry palate**: large - formed by fusion of the horizontal palatine process of the maxilla (one from each side)

N.B. The nasal septum descends vertically to fuse with the upper surface of the palate.



Commonest Anomalies of the face & palate

1. Inclusion dermoid
2. **Macrostoma** (large mouth)
3. **Microstoma** (small mouth)
4. Oblique facial cleft
5. Hare lip: (unilateral & bilateral)
6. Cleft palate: (unilateral complete & bilateral complete & isolated)
7. Bifid soft palate & bifid uvula.

dermoid cyst



inclusion dermoid



Macrostoma



microstoma



oblique facial cleft



hare lip (unilateral)



hare lip (bilateral)



cleft palate (unilateral)



cleft palate (complete)



cleft palate (isolated)



bifid uvula

Summary & Illustrations

Development of Mouth Cavity and Salivary Glands

The Mouth Cavity

The mouth cavity develops from 2 sources:

(i. stomodeum and ii. anterior end of the foregut)

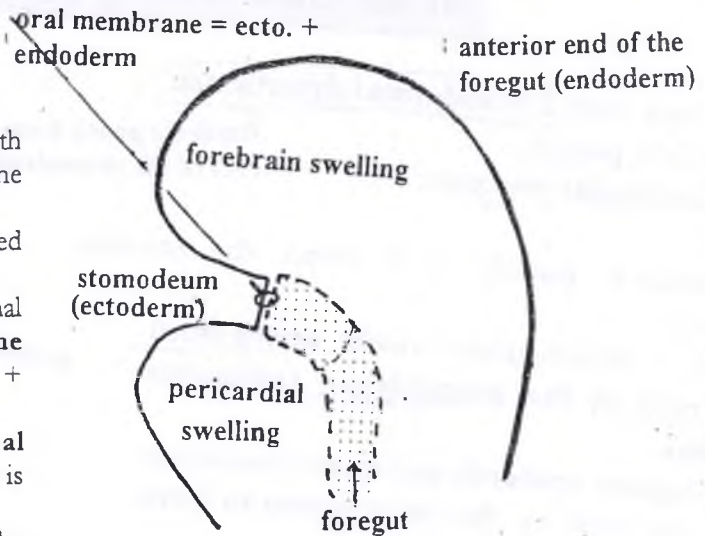
i. The **stomodeum** is a depression lined with **ectoderm**, lies between the frontonasal process and the processes of the 1st pharyngeal arch.

ii. The floor of the **ant. end of foregut** which is lined by **endoderm**.

-The ectodermal **stomodeum** and the endodermal anterior end of **foregut** are separated by the **buccopharyngeal or oral membrane** (ecto + endoderm).

-At the end of the 3rd week the **buccopharyngeal membrane ruptures** & the primitive mouth cavity is formed by the 2 components.

-Formation of the palate separates the mouth from the nasal cavity.



Salivary glands

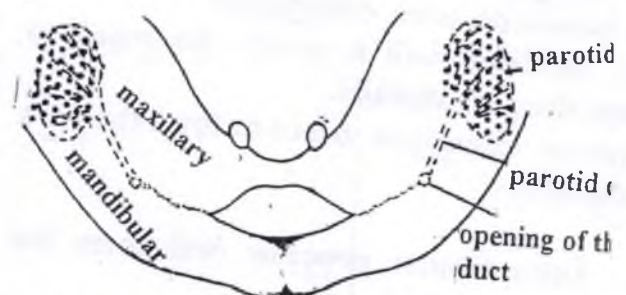
1- Parotid

The gland begins as a **solid ectodermal outgrowth** from the **buccal epithelium** of the inner aspect of the cheek at the junction between the maxillary and mandibular processes of the first arch.

The **distal part of the outgrowth** extends backward to reach a position below the auricle, where it breaks into several buds which form the **acini of the gland**.

The **proximal part of the outgrowth** is canalized to form the **parotid duct**.

The duct recedes from the angle of mouth to open in the vestibule of the mouth opposite the upper 2nd molar tooth.



2- Submandibular:

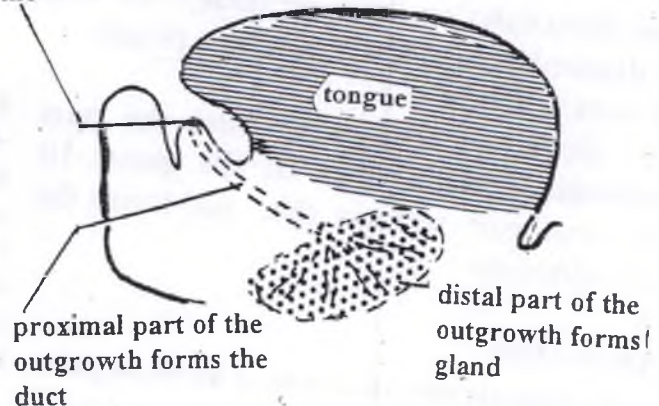
Begins as a **solid endodermal outgrowth** from the **alveolo-lingual groove** which lies between the tongue and the alveolar process, **in the floor of the mouth**.

This outgrowth extends backwards and downwards to a position below the mandible where it breaks into several buds which form the acini of the gland.

The proximal part of the outgrowth is canalized to form the **submandibular duct**.

The anterior end of the duct opens close to the frenulum of the tongue.

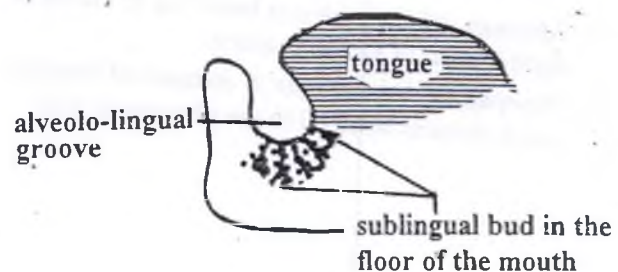
alveolo-lingual groove in the floor of the mouth



3- Sublingual gland

It arises as **small endodermal buds** developing from the **alveolo-lingual groove in the floor of the mouth**.

These buds attain a **common sheath** and appear as one gland having several openings in floor of the mouth.



Summary & Illustrations

Development of Pituitary gland

It develops from 2 ectodermal diverticula:

i. Rathke's pouch.

ii. Infundibular process.

i. Rathke's pouch: (will form the anterior pituitary)

This is a diverticulum which arises from the roof of the stomodeum (primitive mouth).

It elongates upwards and loses connection with the roof of the stomodeum to form the anterior lobe of the gland.

Its posterior wall remains thin and forms the pars intermedia.

Its lumen becomes obliterated.

Its anterior wall is greatly thickened to form the pars distalis.

Upward extensions occur to form the pars tuberalis.

ii. Infundibular process: (will form the posterior pituitary)

This is a diverticulum from the floor of the diencephalon (third ventricle).

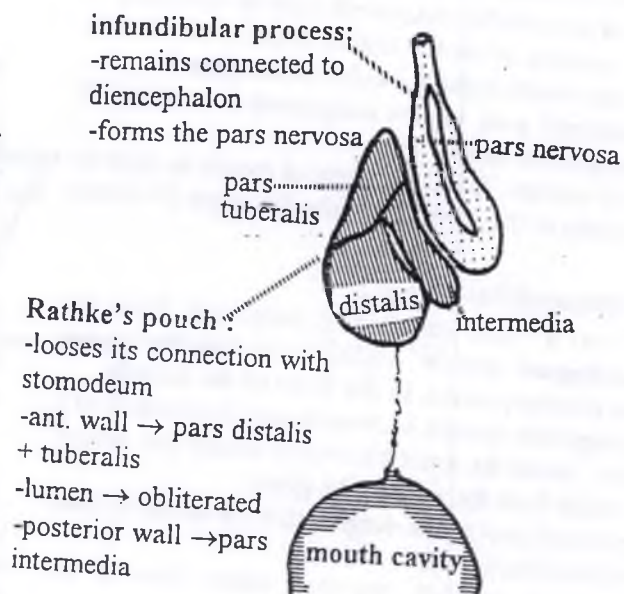
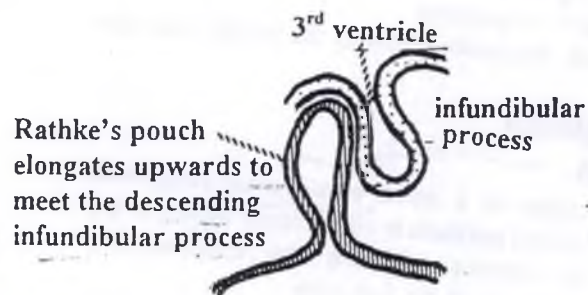
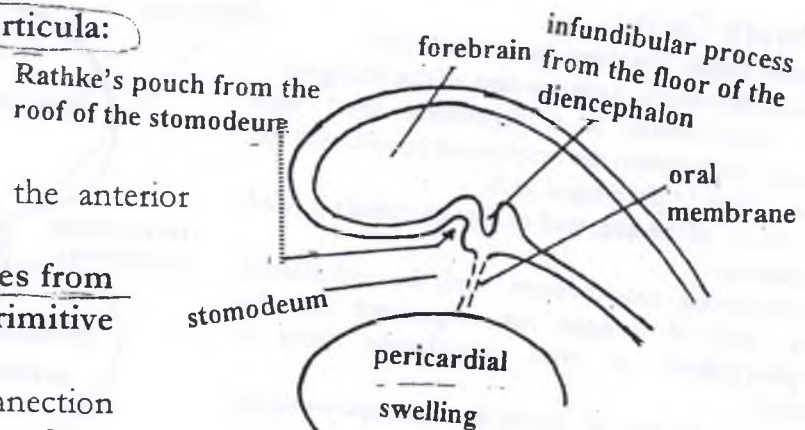
It descends caudal to the Rathke's pouch.

It loses its lumen.

Its distal end enlarges to form the pars nervosa (Posterior lobe of the gland). Its proximal part remains thin and forms the infundibulum.

Anomalies:

- 1- **Agenesis** complete absence of the whole gland.
- 2- **Absence of the anterior lobe**: due to failure of development of Rathke's pouch.
3. **Pharyngeal hypophysis**: A remnant of Rathke's pouch remains attached to the pharyngeal wall.



DEVELOPMENT OF THE RESPIRATORY SYSTEM

Laryngo-tracheal tube:

The respiratory tract arises as a longitudinal groove in the endoderm of the floor of the cranial part of the foregut, termed the laryngo-tracheal groove.

The groove deepens and its edges fuse with each other to form the laryngotracheal tube.

The cranial (anterior) part of the tube becomes the larynx which opens into the pharynx by the laryngeal orifice.

The caudal part separates from the related part of the foregut (future esophagus) and divides into the 2 principal bronchi, each of which is surrounded by a mesodermal mass and is called the lung bud.

The cartilages and muscles of the larynx develop mainly from the mesoderm of the 4th and 6th branchial arches.

The cartilages and muscles of the trachea and bronchi develop from the splanchnic mesoderm which surrounds the laryngo-tracheal tube.

Lung bud:

Each lung bud (endoderm) branches into bronchi, bronchioles and alveoli of the lung.

The surrounding mesoderm forms the stroma and blood vessels of the lung.

The pleura is formed by a part of the intraembryonic coelom.

Commonest Anomalies:

1. **Tracheo-esophageal fistula:** This occurs due to incomplete fusion of the lips of the laryngo-tracheal groove which leads to persistence of a communication (fistula) between the trachea and esophagus. It is generally associated with esophageal atresia (closure). The 4 varieties of fistula are illustrated on page 19.
2. **Abnormal branching of the laryngo-tracheal tube** or the lung bud may lead to:
 - i. **absence** of a lung lobe or to ii. **formation** of an **accessory lobe** or iii. **accessory broncho-pulmonary segment**.

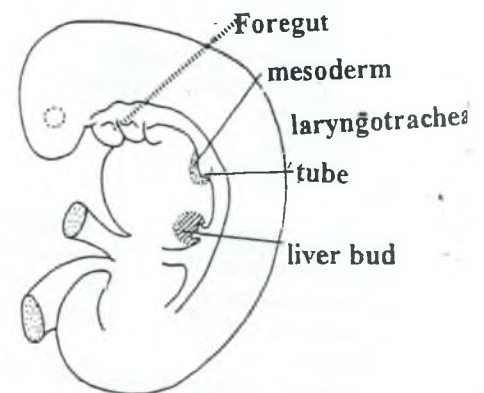
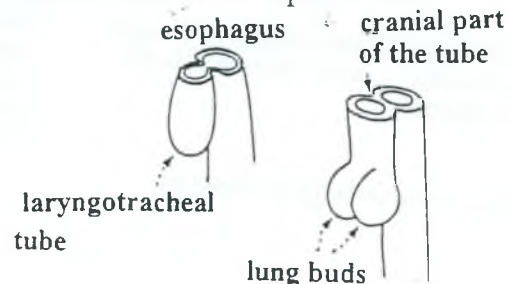
Summary & Illustrations

DEVELOPMENT OF THE RESPIRATORY SYSTEM

Laryngotracheal tube

-The tube starts as a groove in the endoderm of foregut

-The groove is transformed into tube & separated from the esophagus

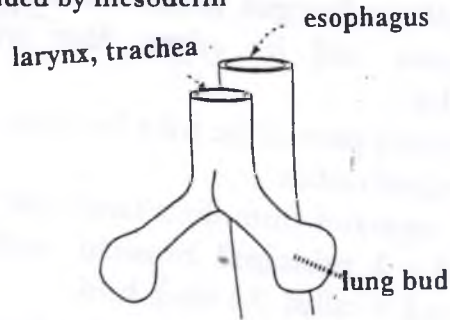
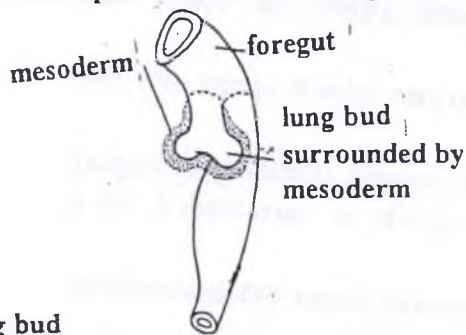


Summary & Illustrations

DEVELOPMENT OF THE RESPIRATORY SYSTEM (continued)

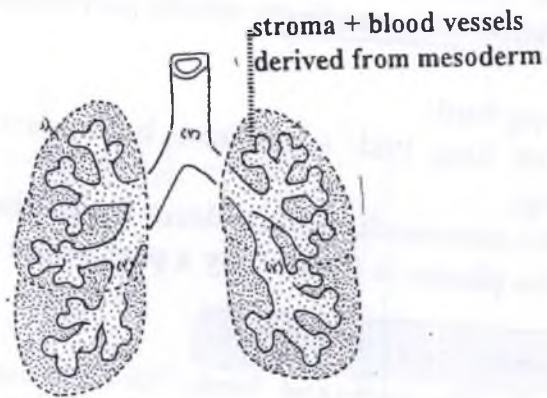
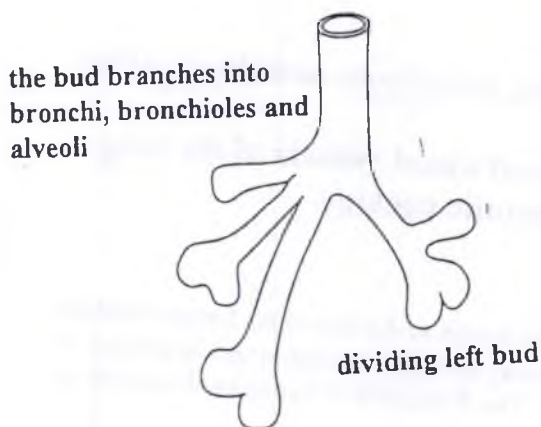
Laryngotracheal tube (continued)

- The cranial part of the tube → larynx & trachea
- The caudal part divides into 2 lung buds surrounded by mesoderm



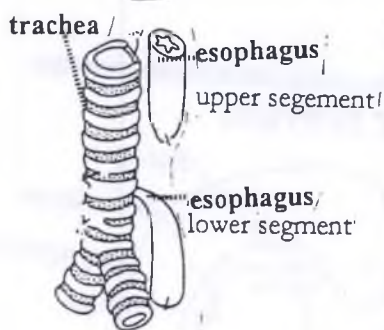
Lung bud

- Each lung bud branches into bronchi, bronchioles & alveoli
- The mesoderm → stroma & blood vessels of the lung
- The intraembryonic coelom → pleura

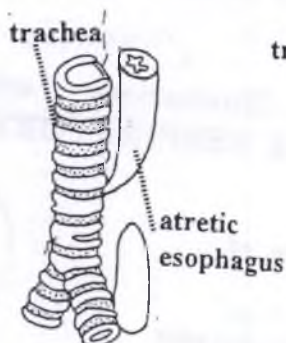


Commonest anomalies

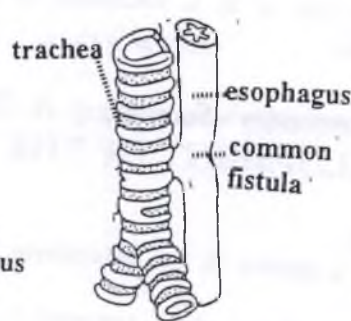
1. Tracheo-esophageal fistula (4 varieties)



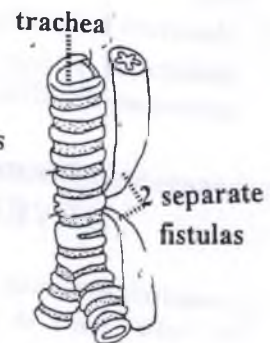
The upper segment of esophagus ends blindly, the lower segment is connected by a fistula to the trachea



The upper segment of esophagus forms a fistula with the trachea, the lower segment of esophagus ends blindly



The 2 segments of esoph. make a common fistula



The upper & lower segments are connected separately to the trachea

2. Abnormal branching of the laryngo-tracheal tube which may lead to:

- Absence of one lobe
- Accessory lobe
- Accessory broncho-pulmonary segment

DEVELOPMENT OF DIGESTIVE SYSTEM

As a result of folding: the cranial part of the yolk sac becomes included in the head fold to form the foregut, the caudal part becomes included in the tail fold to form the hind gut and the middle part becomes included between the 2 lateral folds to form the midgut. The mid gut is connected ventrally by means of the vitello-intestinal duct to the definitive yolk sac.

Derivatives of gut

Part	Artery	Derivatives
A. Foregut Upper part Lower part	Coeliac trunk	Posterior part of buccal cavity. Pharynx and its derivatives. Esophagus, stomach & lower respiratory tract 1 st part of duodenum and upper 1/2 of second part till biliary orifice. Liver, biliary duct system & pancreas.
B. Midgut	Superior mesenteric artery	Lower 1/2 of 2 nd part, 3 rd and 4 th parts of duodenum. Jejunum and Ileum. Cecum and appendix. Ascending colon and right colic flexure. Right 2/3 of transverse colon.
C. Hindgut	Inferior mesenteric artery	Left 1/3 of transverse colon. Left colic flexure. Descending and pelvic colon. Rectum & upper part of anal canal. In addition to most of the epithelium of urinary bladder and of the urethra (from the ventral part of cloaca).

Development of the Pharynx

The cephalic end of foregut i.e. primitive pharynx after the formation of pharyngeal pouches and the development of tongue will become the pharynx.

Development of the Esophagus

The part of foregut caudal to the pharynx (from laryngotracheal groove till stomach) remains tubular and forms the esophagus.

At the 4th week of intrauterine life it is a short tube which elongates to match the growth of the neck and thorax.

The epithelial lining of the esophagus is at first columnar and gradually changes into stratified squamous. The muscles in the upper 2/3rds become striated while in the lower 1/3rd they are non striated like the rest of gut.

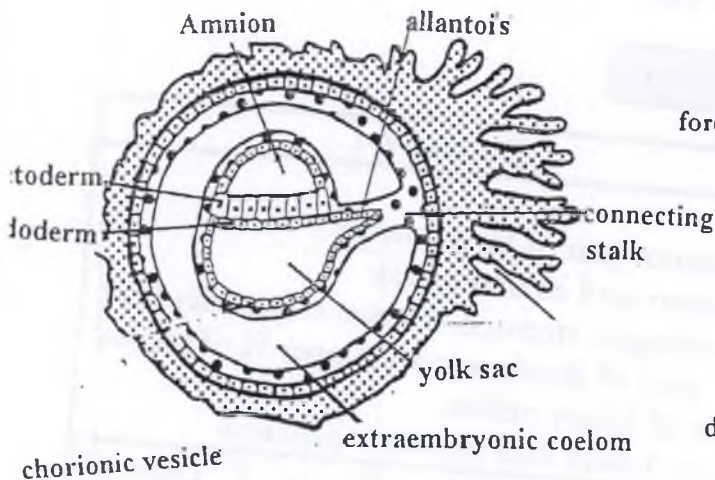
The esophagus has no definite mesentery.

Summary & Illustrations

Development of the digestive system

As a result of folding, the 2ndry yolk sac becomes:

- i. foregut included in the head fold
- ii. hindgut included in the tail fold
- iii. midgut included between the 2 lateral folds



Before folding

The foregut derivatives are:

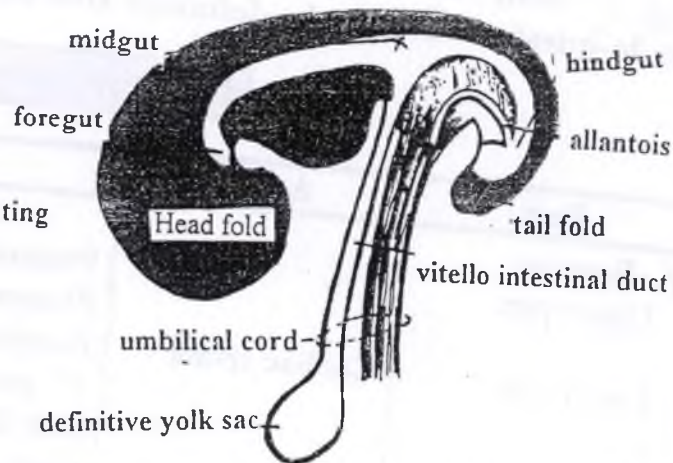
1. posterior part of mouth cavity + pharynx and its derivatives
2. lower part of respiratory trunk
3. esophagus
4. stomach
5. liver
6. pancreas
7. gall bladder
8. biliary duct system
9. 1st part of duodenum and upper 1/2 of the 2nd part till the biliary orifice

Derivatives of the midgut are:

1. the rest of the the duodenum, jejunum and ileum
2. cecum
3. appendix
4. ascending colon
5. right 2/3 of transverse colon

Derivatives of the hindgut are:

1. left 1/3 of transverse colon
2. descending colon
3. sigmoid colon
4. rectum
5. upper part of anal canal
6. most of the epithelium of urinary bladder and urethra



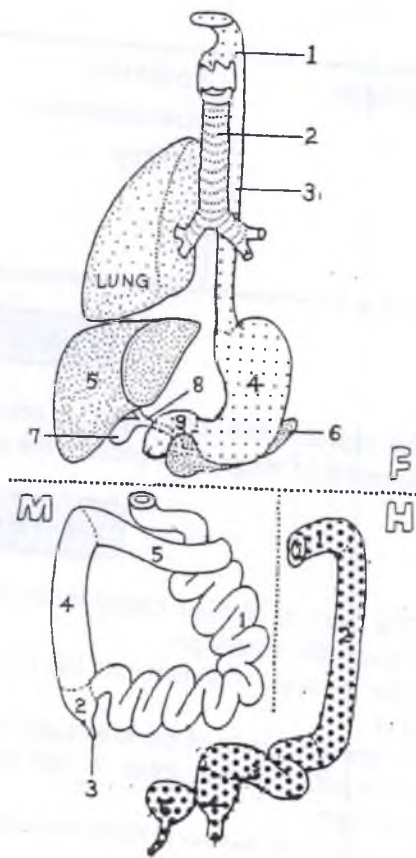
After folding

Derivatives of gut

F foregut derivatives

M midgut derivatives

H hindgut derivatives



Commonest Anomalies:

1. Abnormally short esophagus: In this case the stomach will be intra- thoracic.
2. Abnormally long esophagus:
3. Atresia of the esophagus: In this case the lumen of the esophagus remains obliterated. It is due to failure of recanalisation of the esophagus.
4. Stenosis of the esophagus: It is a local narrowing of the esophagus due to incomplete recanalisation of its lumen.
5. Tracheo-esophageal fistula: It is abnormal communication between the trachea and esophagus. This condition is usually accompanied by esophageal atresia (its 4 varieties are described on pages 18 & 19).

Development of the Stomach

The stomach develops from the endoderm of the foregut.

It shows a fusiform dilatation.

Then, the dilatation increases due to extension of the posterior border which will form the greater curvature.

The anterior border is shorter and will form the lesser curvature. The upper part of this border grows faster to form the fundus.

The posterior border gives attachment to the dorsal mesogastrium.

The anterior border gives attachment to the ventral mesogastrium.

The stomach has two surfaces: right and left surfaces.

Rotation of the Stomach:

The stomach rotates 90° to the right side being pushed by the growing liver.

Results of rotation:

- i. Left surface becomes anterior surface.
- ii. Right surface becomes posterior surface.
- iii. Anterior border forms the lesser curvature.
- iv. Posterior border forms the greater curvature.
- v. The ventral mesogastrium forms the lesser omentum.
- vi. The dorsal mesogastrium forms the gastrophrenic ligament, gastro splenic ligament, lienorenal ligament, and greater omentum.

N.Bs:

1. Being a derivative of the foregut, the stomach is supplied by the coeliac trunk which is the artery of the foregut.
2. As the stomach rotates to the right, the left vagus nerve will be the anterior gastric nerve. While the right vagus nerve will be the posterior gastric nerve.
3. As the stomach rotates to the right a part of the peritoneal cavity is enclosed behind it. This part will be the lesser sac of peritoneum.

Commonest Anomalies:

1- Congenital pyloric stenosis:

The condition is due to abnormal thickening of the pyloric sphincter.

2- Thoracic stomach: This condition is due to abnormal short esophagus.

3- Hour-glass stomach: The stomach shows a local constriction dividing it into 2 parts.

4- Transposition of the stomach: The stomach is transposed into the right side of the abdomen.

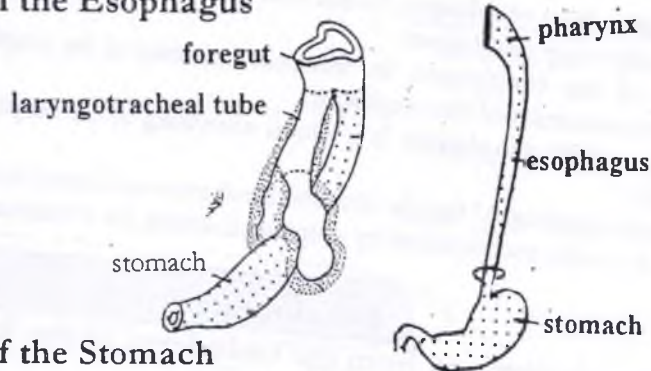
Summary & Illustrations

Development of the Esophagus

Develops from the **endoderm of the foregut** in the area between the inlet of laryngotracheal tube till the stomach.

It remains **tubular in shape** with **no definite mesentery**.

It elongates to match the growth of the neck and thorax.



Development of the Stomach

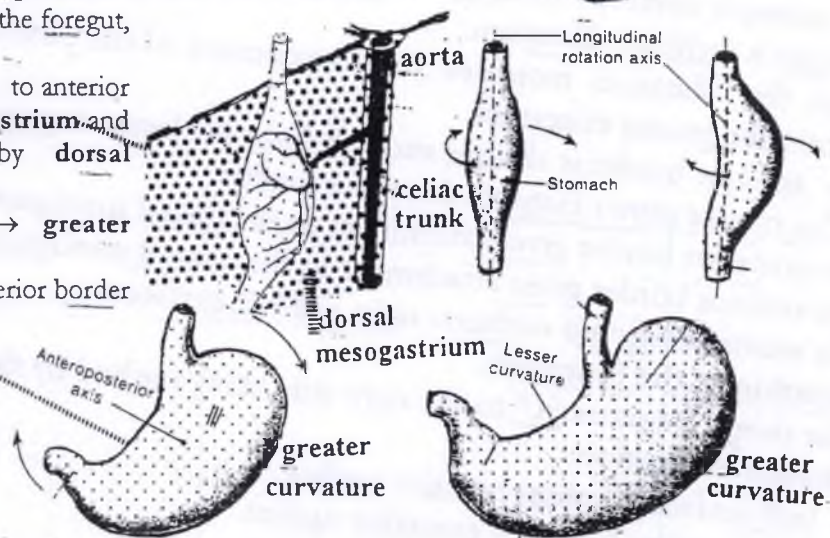
It develops from the **endoderm of the foregut**, supplied by **coeliac trunk**.

It is **fusiform in shape** connected to anterior abdominal wall by **ventral mesogastrium** and to posterior abdominal wall by **dorsal mesogastrium**.

Extension of posterior border → **greater curvature**

Extension of the upper part of posterior border → **fundus**

Anterior border → **lesser curvature**



Rotation of the stomach 90° to the right side results in:

left surface → anterior surface

right surface → posterior surface

right vagus → posterior gastric nerve

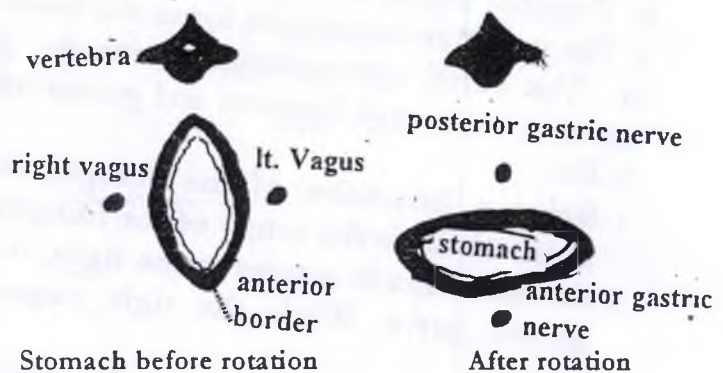
left vagus → anterior gastric nerve

ventral mesogastrium → lesser omentum

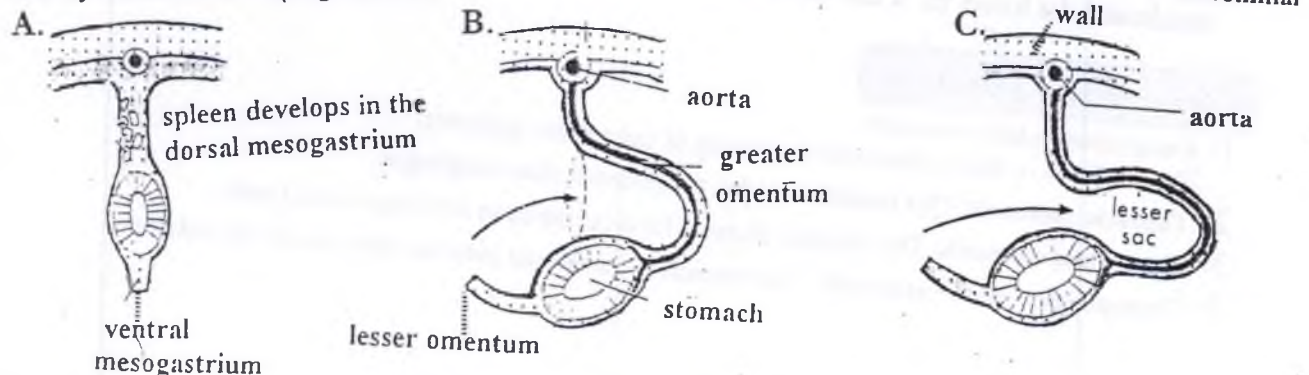
dorsal mesogastrium → gastrophrenic, gastrosplenic ligaments and greater omentum

the lesser sac is enclosed between the anterior and posterior 2 layers of greater omentum.

Changes in the shape of the stomach and development of the curvatures



Development of the lesser sac between the layers of dorsal mesogastrium:



Summary & Illustrations

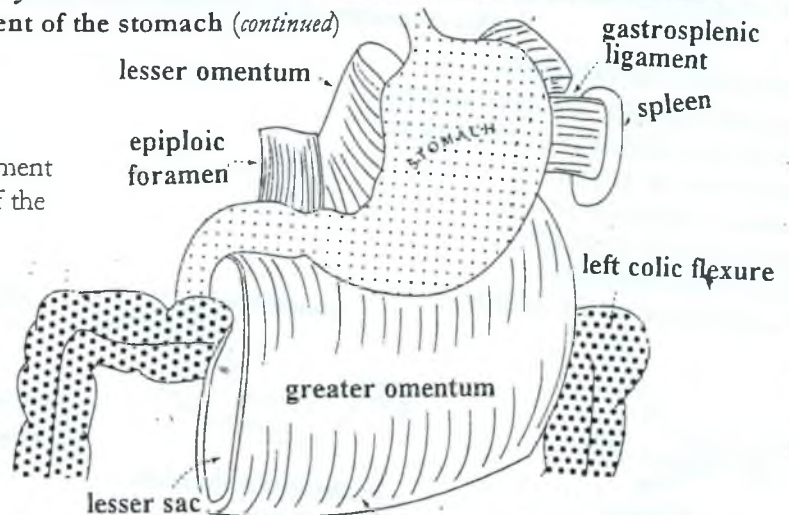
Development of the stomach (continued)

Fate of the dorsal and ventral mesogastria

Ventral mesogastrium → lesser omentum

Dorsal mesogastrium → greater omentum, gastrophrenic, gastrosplenic & lienorenal ligament

lesser sac enclosed between the layers of the greater omentum



Development of the spleen

The spleen arises during the 6th week from mesodermal cells located in the dorsal mesogastrium. These cells form the parenchyma, stroma and capsule of the spleen, which then become infiltrated with hematopoietic cells.

The spleen is supplied by a large splenic artery.

The part of the dorsal mesogastrium between the greater curvature of the stomach and spleen is the Gastro-splenic ligament.

The part of the dorsal mesogastrium between the stomach and left kidney is the lieno-renal ligament.

Development of the Duodenum

Is formed from a loop called duodenal loop.

The upper half of the loop belongs to the endoderm of the foregut, while its lower half belongs to the mid-gut.

The loop is connected to the posterior abdominal wall by dorsal mesentery called the mesoduodenum.

The duodenal loop rotates to the right for 90°, until the duodenum rests on the posterior abdominal wall.

The mesoduodenum fuses with the peritoneum of the posterior abdominal wall, so that most of the duodenum becomes retroperitoneal (behind the peritoneum).

The region of duodenum originating from the foregut is supplied by branches of the coeliac trunk, while that originating from the midgut is supplied by the superior mesenteric artery.

Junction between the foregut and midgut in the adult is just distal to the opening of the bile duct (in the second part of the duodenum).

Commonest Anomalies:

- 1- Atresia of the duodenum: Affects the segment distal to the opening of the bile duct. It is due to obliteration of the lumen, with failure of canalisation.
- 2- Stenosis of the duodenum: due to incomplete recanalisation of a segment of the duodenum.

Summary & Illustrations

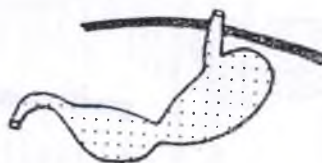
Development of the stomach (continued)

Commonest Anomalies

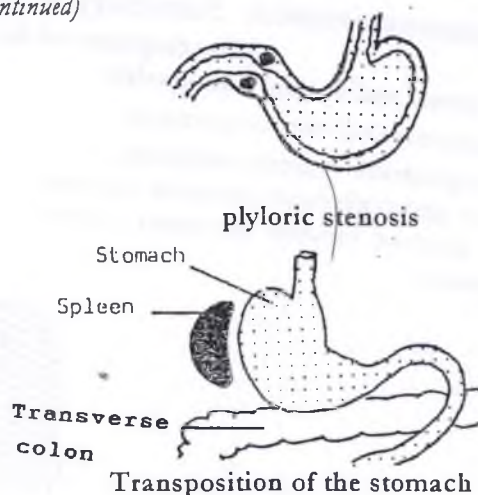
1. **Congenital pyloric stenosis:** abnormal hypertrophy (thickening) of the pyloric sphincter of the stomach
2. **Thoracic stomach:** due to abnormal short esophagus
3. **Hour-Glass stomach.**
4. **Transposition of the stomach.**



Thoracic stomach



Hour glass stomach



Transposition of the stomach

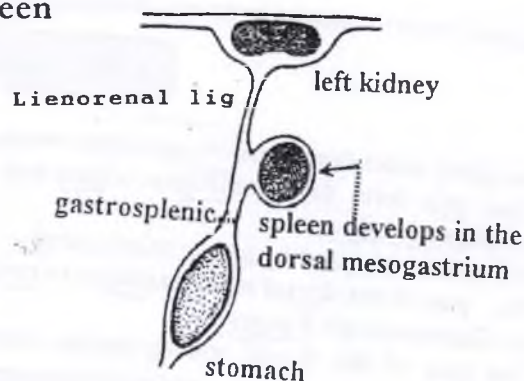
Development of the Spleen

It is developed from mesodermal cells in the dorsal mesogastrium.

These cells will form the stroma and capsule.

Haemopoietic tissue infiltrates the spleen.

The dorsal mesogastrium connected to the spleen will be the gastrosplenic and lienorenal ligaments.



Development of the Duodenum

develops from the duodenal loop.

the upper half of the loop belongs to the endoderm of the foregut.

the lower half belongs to the endoderm of the midgut.

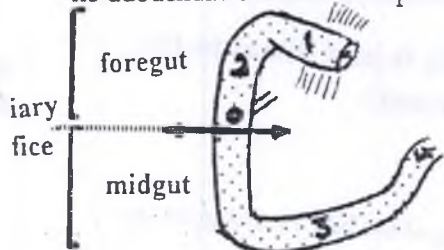
its upper part is supplied by coeliac trunk.

Its lower part is supplied by the superior mesenteric artery.

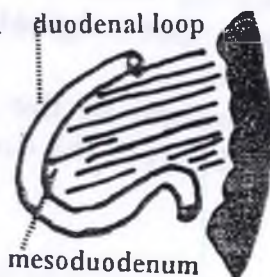
the junction between the 2 parts is just distal to the opening of the bile duct.

rotation of the duodenal loop occurs 90° to the right.

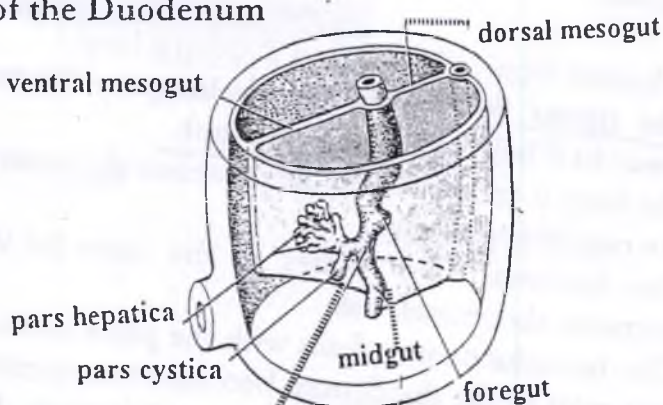
the duodenum becomes retroperitoneal.



Junction between fore- and midgut at the biliary orifice



Duodenal loop is connected to post. abdominal wall by mesoduodenum



The duodenal loop as it develops from the fore- and midgut



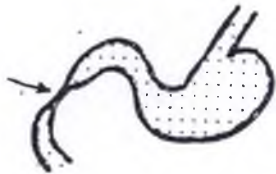
Rotation of the duodenum 90° to the right

Summary & Illustrations

Midgut loop (continued)

The mesoduodenum is absorbed and the duodenum becomes retroperitoneal.

Commonest Anomalies:



1. **Atresia of the duodenum** (failure of canalization) occurs in the segment distal to the opening of the bile duct.



2. **Stenosis of the duodenum**

Mid-Gut Loop (Intestinal Loop)

At the beginning of the 5th week, the greater part of the mid gut forms a U-shaped loop called **intestinal loop**.

The cranial end of the loop is at the duodeno-Jejunal flexure.

The caudal end of the loop is at the junction of the right two thirds with the left third of the transverse colon.

The apex of the loop is connected to the **vitello-intestinal duct**.

This duct connects the intestinal loop with the definitive yolk sac.

The proximal part of the loop is called the **cranial limb**; while the part distal to the vitello-intestinal duct is called the **caudal limb**.

At the 6th week the loop elongates greatly and bulges out within umbilical cord (**physiological umbilical hernia**).

A diverticulum arises from the caudal limb. This is called **cecal bud** because it will form the cecum and vermiform appendix.

At the 10th week the abdominal cavity enlarges leading to reduction of the physiological hernia. At the same time the loop rotates 180° in an anticlockwise direction. This rotation occurs around an axis formed by the superior mesenteric artery (artery of mid gut).

Now the caudal limb lies upwards while the cranial limb lies downwards.

The cranial segment increases greatly in length to form coils of jejunum and ileum.

Rotation increases up to 270°, so that cecum now lies just below liver (sub hepatic).

The vitello-intestinal duct is obliterated & degenerated losing connection with gut.

The cecum then migrates downwards to the right iliac fossa resulting in the formation of the ascending colon.

The mesentery of the ascending colon is absorbed so that it becomes retroperitoneal.

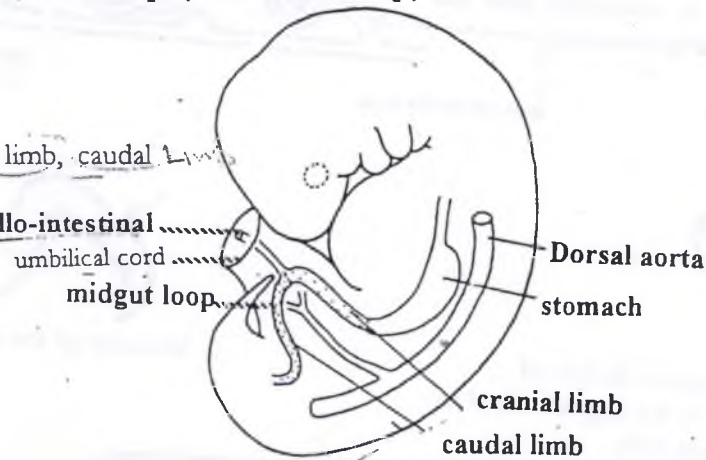
The derivatives of the intestinal loop are: the Jejunum, ileum, cecum, vermiform appendix, ascending colon, right colic flexure and right two thirds of the transverse colon. **These parts are supplied by the superior mesenteric artery.**

cecu
subhepat

Summary & Illustrations

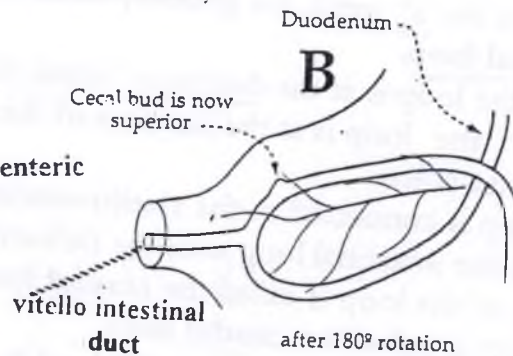
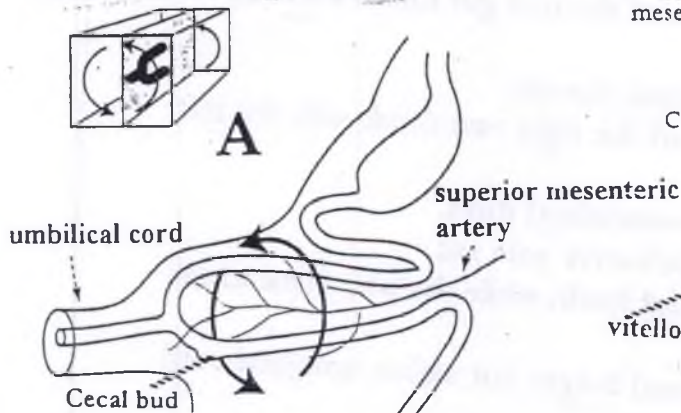
Mid-Gut loop (intestinal loop)

U-shaped loop formed of cranial limb, caudal limb and apex.
The apex is connected to the **vitello-intestinal duct**.



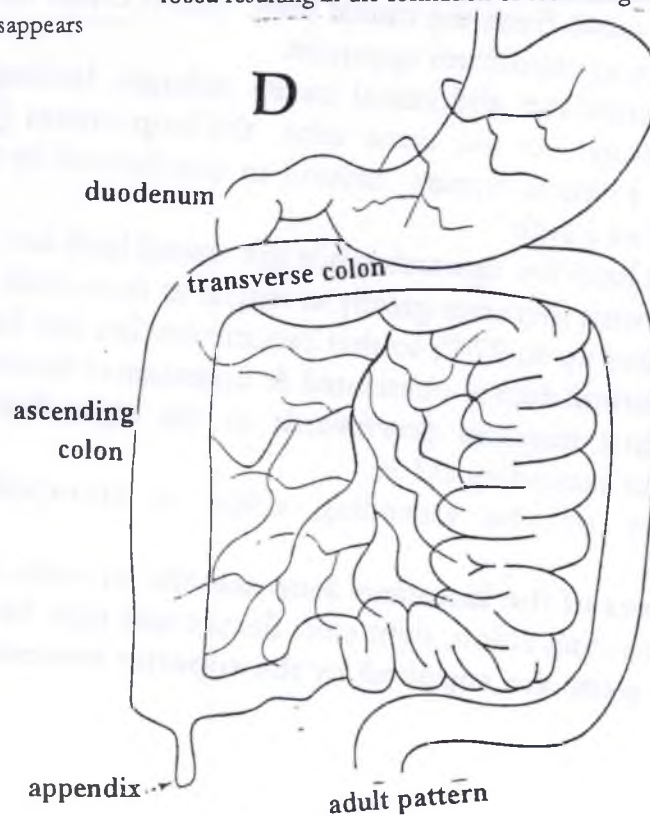
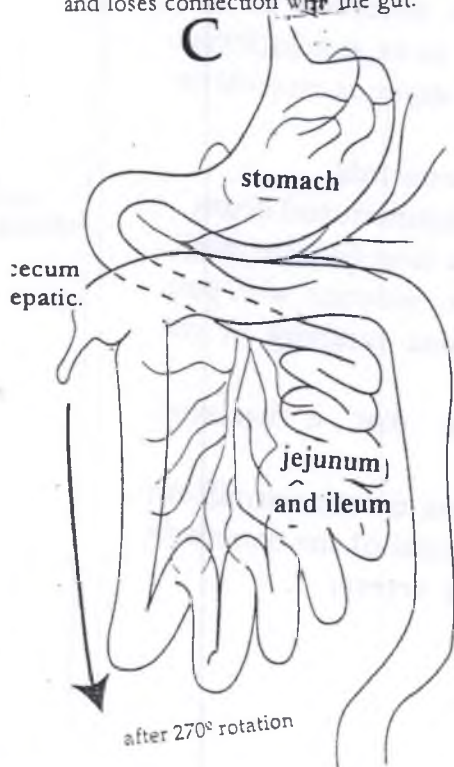
A. At the 6th week, the loop bulges out within the umbilical cord (**physiological umbilical hernia**). Cecal bud appears in the caudal limb.

B. At the 10th week, reduction of the hernia occurs and rotation occurs 180° in anti-clock wise direction around an axis formed of the superior mesenteric artery.



C. Rotation increases up to 270° so that the cecum becomes subhepatic. The vitello-intestinal duct is obliterated, disappears and loses connection with the gut.

D. The cecum migrates downwards to the right iliac fossa resulting in the formation of ascending colon.

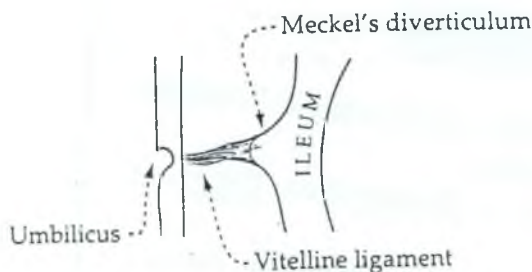


Commonest Anomalies

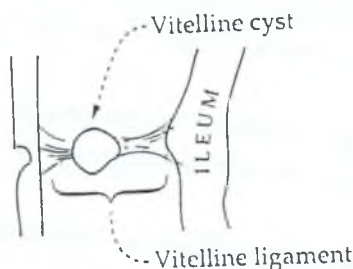
- (1) **Meckel's "ileal" diverticulum:** The vitello-intestinal duct normally becomes obliterated and disappears completely. Sometimes its proximal part near the ileum remains patent forming Meckel's diverticulum. Meckel's diverticulum is 2 inches long, present in 2% of people, attached to the ileum 2 feet from the ileocecal valve.
- (2) **Congenital fecal umbilical fistula:** The whole vitello-intestinal duct remains open forming a direct connection between the intestine and umbilicus (fecal fistula).
- (3) **Vitelline cyst:** Both ends of the vitello-intestinal duct change into fibrous cords while its middle part remains patent forming a cyst.
- (4) **Non-return of the herniated midgut (Omphalocele)** Loops of small intestine may remain inside the umbilical cord at birth due to failure of reduction of the physiological hernia (Congenital umbilical hernia).
- (5) **Atresia & stenosis of any part of the primitive intestinal loop:** Stenosis may affect any part of the primitive loop, most commonly the duodenum.
- (6) **Subhepatic position of the cecum and appendix:** This is due to failure of migration of the cecum down to the right iliac fossa and the ascending colon is not developed.
- (7) **Non-rotation of midgut loop:** The small intestine comes to lie on the right side and the large intestine on the left side.
- (8) **Retro-duodenal transverse colon:** Due to partially malrotated (clockwise) midgut loop. In this case, the duodenum is anterior to the colon.
- (9) **Left sided cecum and appendix:** Due to complete malrotated midgut loop (clockwise direction). Usually this condition is a part of generalised situs inversus (transposition of thoracic & abdominal viscera).

Summary & Illustrations

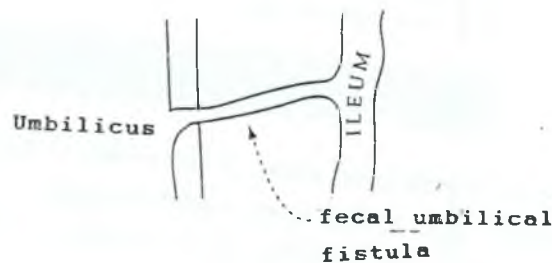
Anomalies of the mid-gut loop



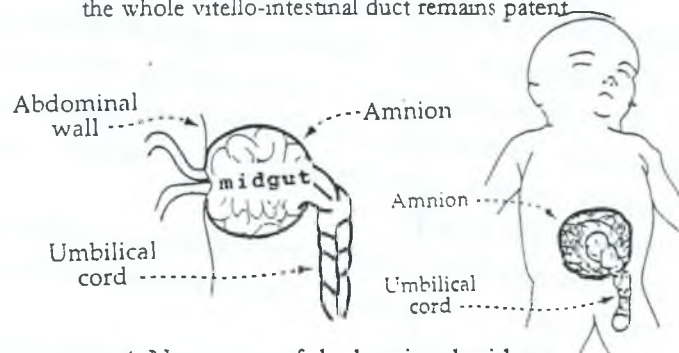
1. Meckel's (ileal) diverticulum: non obliteration of the proximal part of the vitello intestinal duct.



3. Vitelline cyst: only the middle part of the vitello-intestinal duct remains patent.



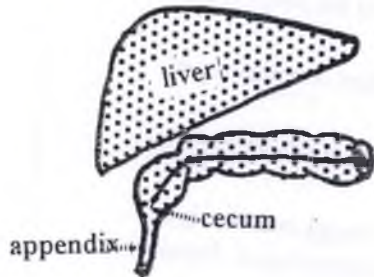
2. Congenital fecal umbilical fistula: the whole vitello-intestinal duct remains patent



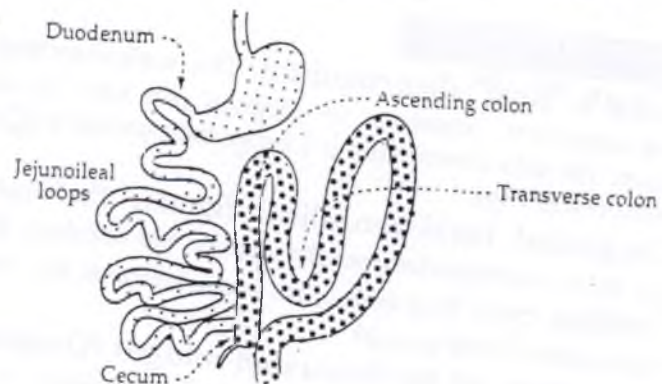
4. Non return of the herniated midgut (omphalocele)

Summary & Illustrations

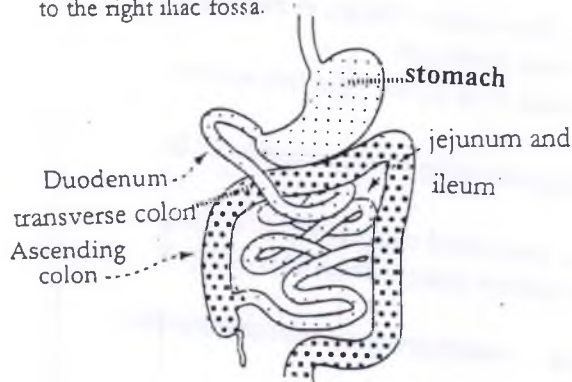
Anomalies of the midgut loop (continued)



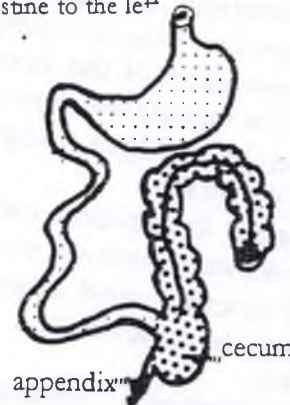
5. subhepatic position of the cecum and appendix. Failure of downward migration to the right iliac fossa.



6. non rotation of mid gut loop. Small intestine to the right and large intestine to the left



7. retroduodenal transverse colon: The duodenum is anterior to the colon due to partial clockwise rotation of the mid gut loop.



8. left sided cecum and appendix, due to complete clockwise rotation of the mid gut loop.

Development of the Liver and Gall Bladder

The liver is developed from 3 sources; 1) Liver bud (endoderm), 2) Vitelline vein (mesoderm) and 3) Septum transversum (mesoderm).

1. The liver bud or hepatic diverticulum begins as a diverticulum from the convexity of the duodenal loop.

It elongates up into the ventral mesogastrium (derived from the septum transversum) and divides into two branches:

i. Pars cystica: which forms the gall bladder and cystic duct.

ii. Pars hepatica: which gives rise to two branches which will later form the right and left hepatic ducts. These ducts branch repeatedly inside the substance of the septum transversum forming the biliary system. Their terminal parts form the cords of liver cells.

2. The vitelline veins which develop in the mesoderm of the septum transversum break into a network of blood sinusoids in the septum transversum between the cords of liver cells.

3. The mesoderm of the septum transversum gives rise to the fibrous stroma and capsule of the liver.

Anomalies:

1. **Atresia of the gall bladder & Atresia of the bile duct:** These cases occur due to failure of the gall bladder and or the bile duct to canalise.
2. **Absent gall bladder:** Due to failure of the par cystica to develop from the liver bud.
3. **Intrahepatic gall bladder:** The gall bladder may be completely embedded inside the liver substance.
4. **Bifid gall bladder:** The fundus and part of the body of the bladder are divided into 2 parts.
5. **Double gall bladder:** Due to division of the pars cystica into 2 branches.
6. **Mobile gall bladder:** It is the suspension of the gall bladder from the liver by a mesentry.

Development of the Pancreas

The pancreas develops from 2 buds or diverticula: 1. ventral pancreas and 2. dorsal pancreas.

1. Ventral pancreas:

Develops as a diverticulum from the endoderm of the proximal part of the liver bud.

As it grows it migrates on the right side of the duodenum to reach the concavity of the duodenum.

It forms the lower part of the head and the uncinat process of pancreas.

2. Dorsal pancreas:

Develops as a diverticulum from the endoderm of the concavity of the duodenum.

It is enlarged greatly to form the tail, body, and upper part of the head of pancreas.

Pancreatic ducts:

Later on, the ducts of the dorsal & ventral pancreas join each other to form the main pancreatic duct. It is formed in its distal part by the duct of dorsal pancreas and in its proximal part by the duct of ventral pancreas. The main pancreatic duct is joined by the common bile duct to form the **hepato-pancreatic ampulla of Vater**. The latter opens in the 2nd part of the duodenum.

The proximal part of the dorsal pancreatic duct is usually obliterated, but occasionally it remains patent forming the **accessory pancreatic duct**.

Anomalies:

1. **Accessory pancreas:** A mass of pancreatic tissue may invade the pyloric portion of the stomach to lie in its submucosa.
2. **Annular pancreas:** a ring of pancreatic tissue surrounds the whole circumference of the duodenum due to abnormal migration of the pancreatic buds.
3. **Cystic fibrosis of pancreas:** due to abnormal viscous pancreatic secretions.
This will lead to obstruction of the pancreatic duct → cyst formation + fibrosis of the pancreatic tissue.
4. **Absent ventral pancreatic duct:** sometimes the duct of ventral pancreas is absent and cannot complete the main pancreatic duct. In this case the duct of the dorsal pancreas acts as the only pancreatic duct. It opens separately into the duodenum above the bile duct. The bile duct opens also separately into the duodenum.

Summary & Illustrations Development of the liver

The liver is developed from 3 sources:

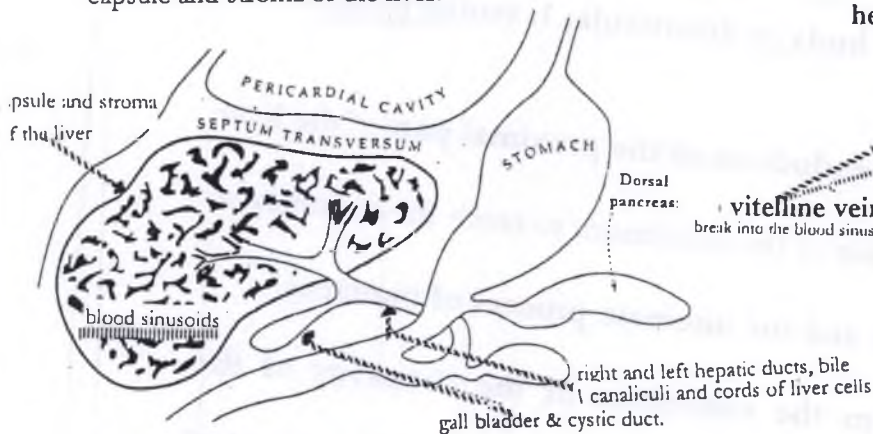
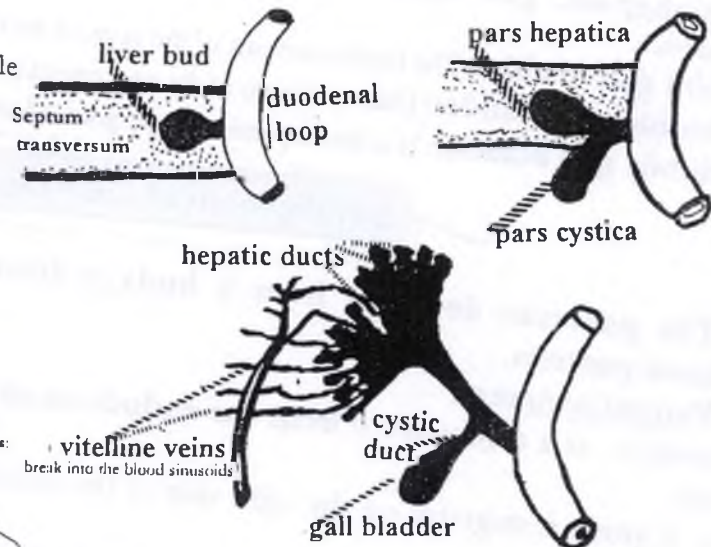
1. Liver bud (endoderm) 2. Vitelline veins (mesoderm) 3. Septum transversum (mesoderm)

1. The liver bud: a diverticulum from the convexity of the duodenum divides into:

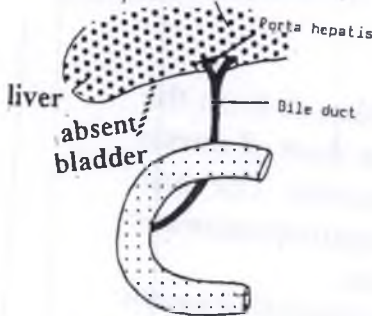
- i. pars cystica → gall bladder & cystic duct.
- ii. pars hepatica → right and left hepatic ducts, bile canaliculi and cords of liver cells.

2. Vitelline veins: break into the blood sinusoids between the cords of liver cells.

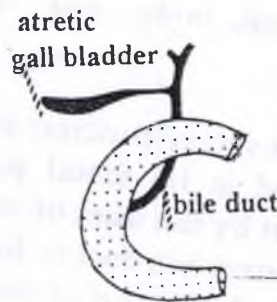
3. Septum transversum: gives the fibrous capsule and stroma of the liver.



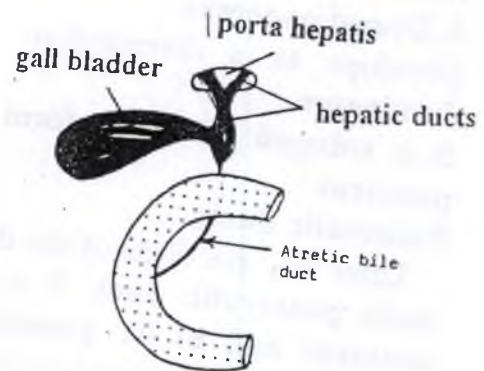
Commonest anomalies:



1. Absent gall bladder
failure of the pars cystica to develop



2. Atresia of the gall bladder
failure of canalization



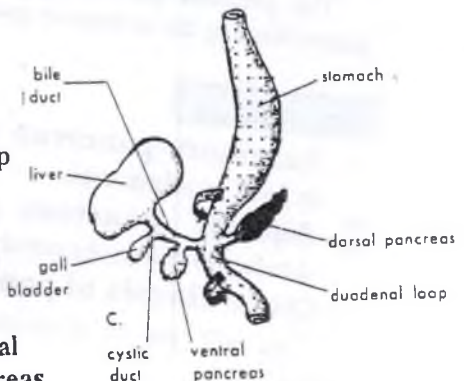
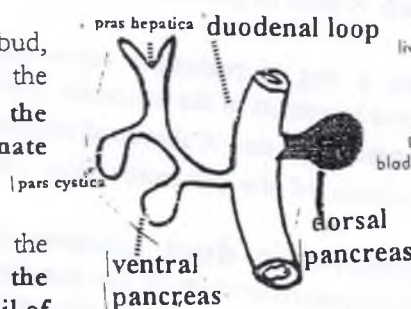
3. Atresia of the bile duct
failure of canalization

Development of the Pancreas

-Develops from 2 buds (i. ventral and ii. dorsal)

i. Ventral pancreas: arises from the liver bud, migrates from the convexity into the concavity of the duodenum → forms the lower part of the head and uncinate process of the pancreas.

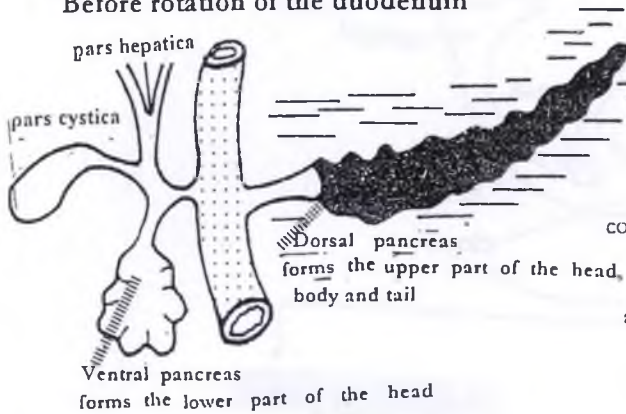
ii. Dorsal pancreas: arises directly from the concavity of the duodenum, forms the upper part of the head, body and tail of the pancreas.



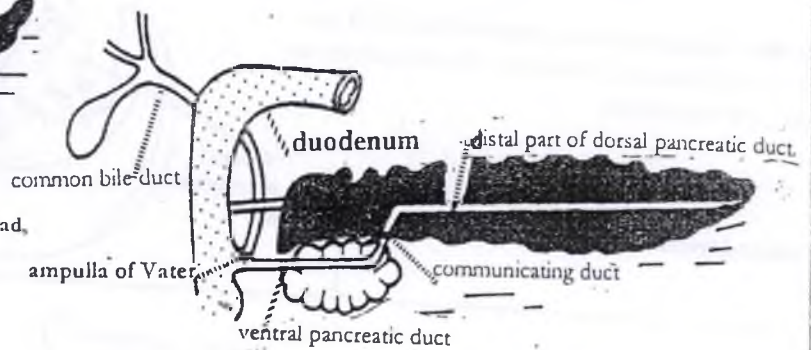
Summary & Illustrations

Development of the pancreas (continued)

Before rotation of the duodenum



After rotation of the duodenum

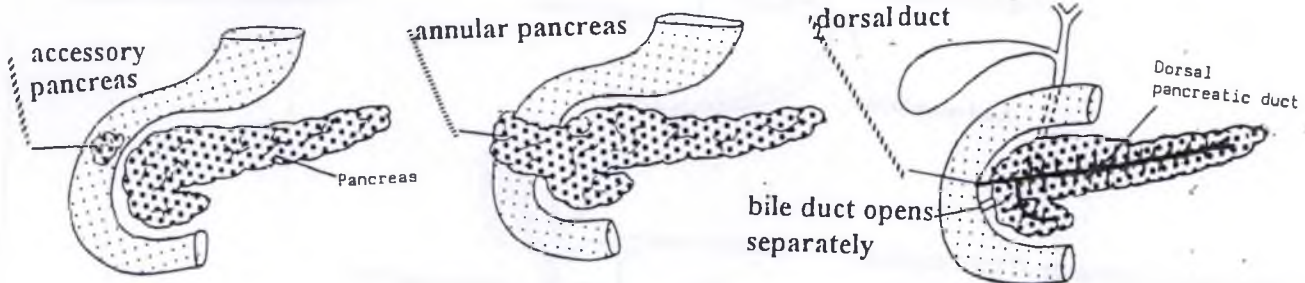


The main pancreatic duct:

-Is formed of the ventral pancreatic duct + communicating duct + distal part of dorsal pancreatic duct.

-It is joined by the common bile duct to form **ampulla of Vater** which opens in the 2nd part of the duodenum.

Commonest anomalies:



1. **Accessory pancreas**
pancreatic tissue invades
submucosa of the stomach

2. **Annular pancreas**
a ring of pancreatic
tissue surrounds duodenum

3. **Absent ventral pancreatic duct**
the dorsal duct opens separately above
the bile duct

Hindgut

Its derivatives are: left third of transverse colon, left colic flexure, descending colon, sigmoid (pelvic) colon, rectum and upper 1/2 of anal canal (illustrations on page 21).

These parts are **supplied by the inferior mesenteric artery** (artery of hind gut).

The terminal part of the hind gut dilates to form the **cloaca**.

The cloaca

It is the terminal expanded part of hindgut distal to point of connection to allantois.

The cloaca is connected to the umbilicus by the allantois and is closed below by the **cloacal membrane** which is bilaminar i.e. **formed of 2 layers:** (i) outer **ectodermal** layer & (ii) inner **endodermal** layer.

The **mesoderm at the angle between the allantois and the cloaca** proliferates to form the "**urorectal septum**" which descends towards the cloacal membrane, thus **dividing the cloaca into 2 parts:**

-**Primitive urogenital sinus: ventrally.**

-**Anorectal canal, dorsally** (which gives the rectum and upper part of the anal canal)

The urorectal septum comes in contact with the cloacal membrane and divides it into 2 parts:

i) **Urogenital membrane: ventrally.** ii) **Anal membrane: dorsally.**

The **primitive urogenital sinus** is subdivided by the point of entrance of mesonephric ducts into 2 parts:

A) **Vesico-urethral canal:** is the cranial part which has the allantois attached to its apex. It forms:

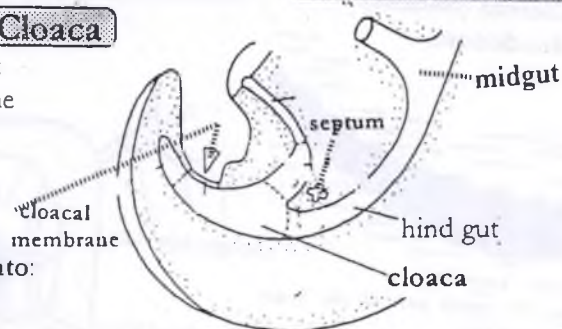
The urinary bladder (except the trigone) in male and female, upper part of the prostatic urethra in male and the whole urethra in female.

Summary & Illustrations

Cloaca

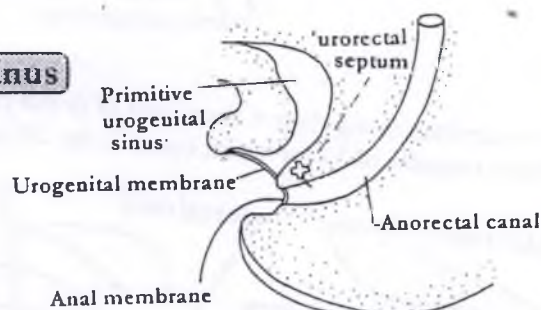
- It is the expanded distal part of the hind gut
- It is closed below by bilaminar cloacal membrane (endo., and ectoderm).

-A mesodermal urorectal septum divides it into:



Primitive urogenital sinus

ventrally

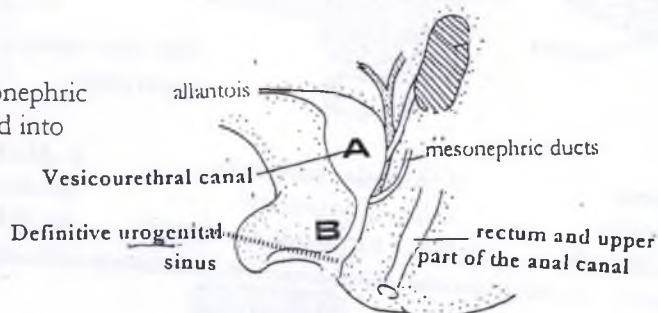


Anorectal canal

dorsally

gives the rectum and upper part of the anal canal

- At the point of entrance of mesonephric duct the urogenital sinus divided into 2 parts:



A. Vesicourethral canal

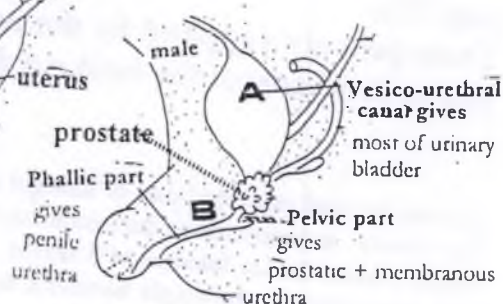
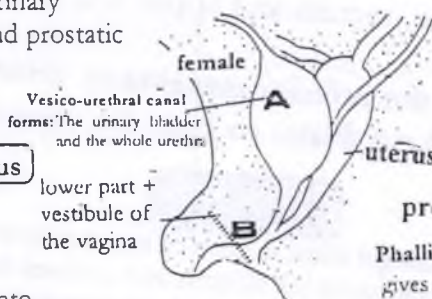
cranially,
which gives:

- | | |
|---|---|
| in female | in male |
| most of urinary bladder and whole urethra | most of urinary bladder and prostatic urethra |

B. Definitive urogenital sinus

caudally,
which gives:

- | | |
|--------------------------------------|--|
| in female | in male |
| lower part + vestibule of the vagina | it is divided into |
| | i. Pelvic part gives part of prostatic + membranous urethra |
| | ii. Phallic part gives most of the penile urethra |



Cloaca (continued)

B) Definitive urogenital sinus: is the caudal part (caudal to the opening of the mesonephric ducts).
In male it is divided into: i. upper (**pelvic**) part which gives the lower part of prostatic & membranous urethra, and ii. lower (phallic) part which gives the major part of penile urethra.
In female it gives the lower part & vestibule of the vagina.

Development of Rectum and Anal canal

- The rectum and upper part of the anal canal develop from the dorsal part of the cloaca, which is called the anorectal canal (endoderm). It is closed by the anal membrane. This membrane is bilaminar: formed of outer ectodermal layer and inner endodermal layer.
- The lower part of anal canal develops from the "proctodeum" which is an ectodermal depression caused by proliferation of the mesoderm surrounding the anal membrane. It is separated from the upper part of anal canal by the anal membrane.

The anal membrane breaks (in the 9th week) and the two parts of the anal canal become continuous with each other.

N.B. The line of demarcation between ecto- and endodermal parts of the anal canal is the "pectinate line" which marks the site of the former "anal membrane".

Correlation between the anatomy of the anal canal and its development

The rectum and upper part of anal canal is endodermal in origin lined with simple columnar epithelium, has smooth muscle fibres, supplied by superior rectal artery (artery of the hind gut), drained by the portal venous system and innervated by the autonomic nervous system. However, the lower part of the anal canal is ectodermal in origin, lined with stratified squamous epithelium, has striated muscle fibres, supplied by systemic rectal arteries (middle & inferior rectal arteries), drained by the systemic venous system and innervated by the somatic nervous system.

Anomalies of the Rectum and anal canal

- 1) **Imperforate anus:** Due to failure of rupture of the anal membrane (between the endodermal and ectodermal parts of the anal canal).
- 2) **Atresia of rectum:** Due to failure of development of the proctodeum, the rectum ends blindly & is separated from the surface by a mass of connective tissue.
- 3) **Recto-urinary fistula & 4) Recto-vaginal fistula:**

They are seen frequently with imperforate anus and are caused by incomplete division of the cloaca into 2 parts so, the rectum remains connected to the urinary bladder, urethra or vagina.

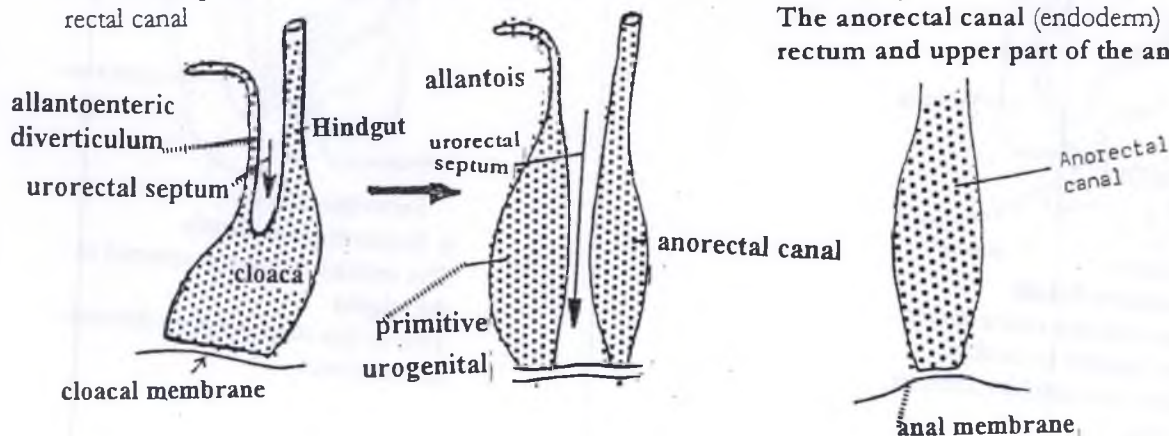
Summary & Illustrations

Development of the Rectum and Anal Canal

The rectum and anal canal are developed from i. anorectal canal, ii. proctodeum (endo- + ectoderm)

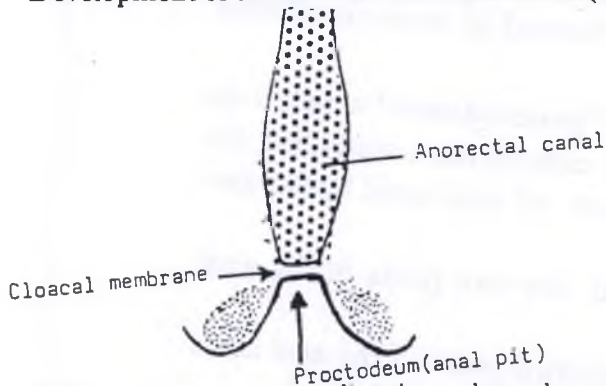
i. Mesodermal urorectal septum divides cloaca into ventral primitive urogenital sinus and dorsal anorectal canal

ii. The anorectal canal (dorsal part of the cloaca) is closed by anal membrane (ecto- + endoderm). The anorectal canal (endoderm) gives the rectum and upper part of the anal canal

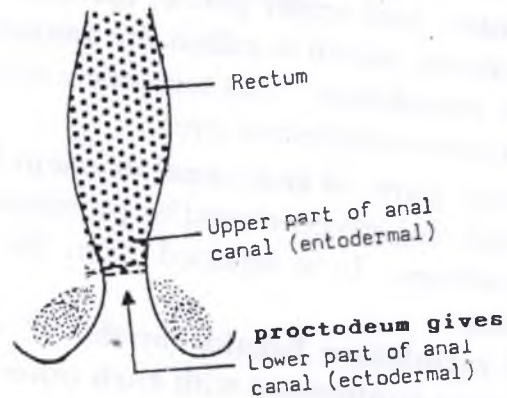


Summary & Illustrations

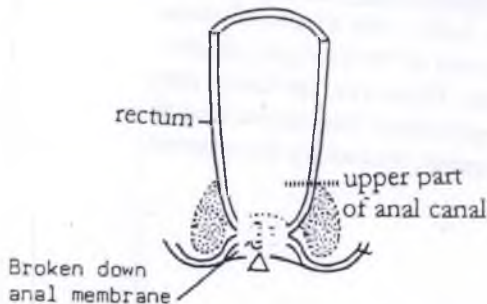
Development of the Rectum and Anal Canal (continued)



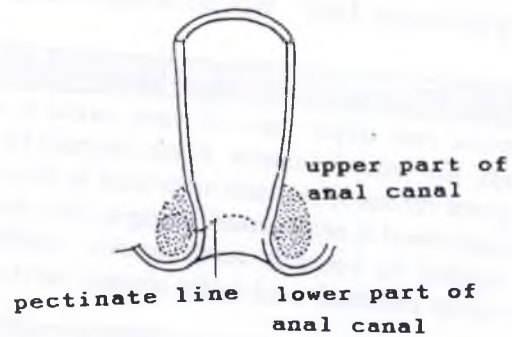
iii. The mesoderm surrounding the anal membrane proliferates causing an **ectodermal depression** called **proctodeum**



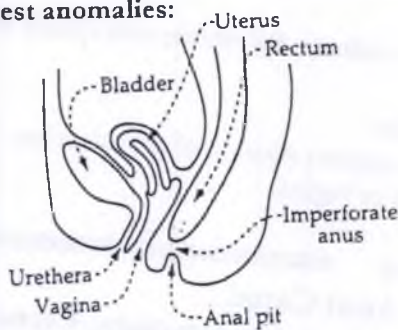
iv. The **proctodeum** (ectoderm) → lower part (1/3) of the anal canal



v. The **anal membrane breaks** and the 2 parts of the anal canal become continuous with each other
Commonest anomalies:

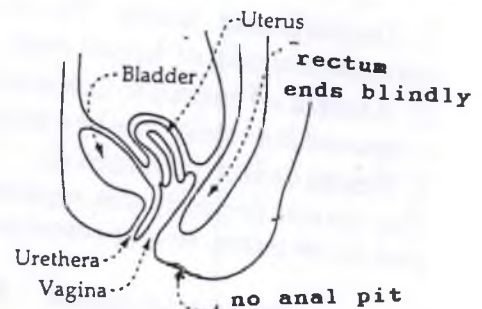


vi. The line of separation between the 2 (ecto- & endodermal) parts is the **pectinate line**



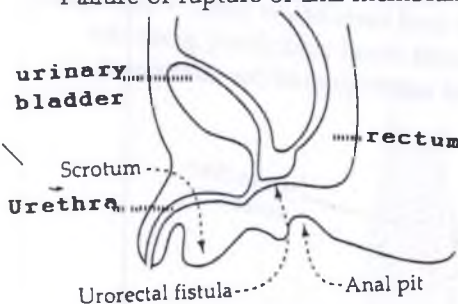
1. Imperforate anus

Failure of rupture of anal membrane



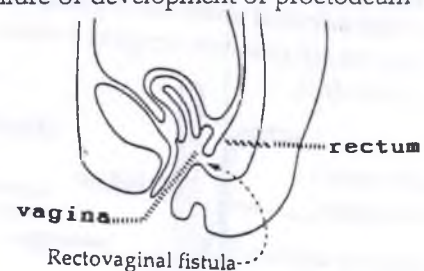
2. Atresia of the rectum

The rectum ends blindly due to failure of development of proctodeum



3. Rectourinary fistula

The rectum remains connected to the urinary bladder or urethra
This is due to incomplete division of the cloaca.



4. Rectovaginal fistula

The rectum remains connected to the vagina
This is due to incomplete division of the cloaca

DEVELOPMENT OF THE URINARY SYSTEM

Development of the kidney *short*

The kidneys develop from the intermediate cell mass of mesoderm (nephrogenic cord).

The development of the human kidney passes in 3 stages: A.) pronephros, B.) mesonephros and C.) metanephros.

These 3 stages appear one after the other (in time), in addition to being situated one caudal to the other. The earlier stages of development (pro- and mesonephros) degenerates or becomes transformed into some form of ducts before the appearance of the succeeding stage.

A. Pronephros

- appears in the upper part of the intermediate mesoderm (in cervical region).
- about 5-7 pronephric tubules are formed.
- Each tubule opens into the intraembryonic coelom.
- The other ends of the tubules open into the pronephric duct (later mesonephric duct). This duct opens into the cloaca.
- The pronephric tubules do not function & by the 4th week they degenerate completely in man. The pronephric duct persists as mesonephric duct.

B. Mesonephros *short*

- Appears in the middle part of the intermediate mesoderm.
- 70-80 S-shaped mesonephric tubules are formed.
- Each mesonephric tubule becomes invaginated by a branch of dorsal aorta and forms an internal glomerulus at one end, at the other end it opens into the mesonephric duct (Wolfian duct).
- The mesonephros excretes urine during embryonic and early fetal periods only.
- By the end of the 2nd month it differentiates into many derivatives.

Summary & Illustrations

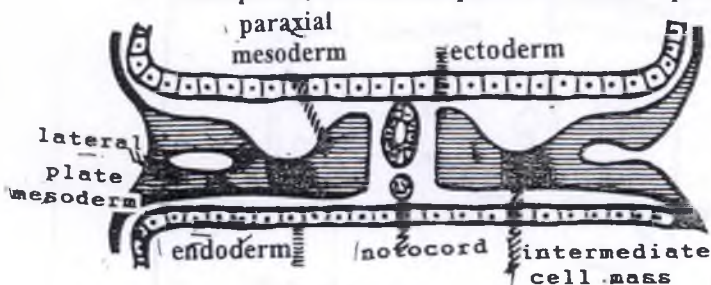
DEVELOPMENT OF THE URINARY SYSTEM

Development of the kidney

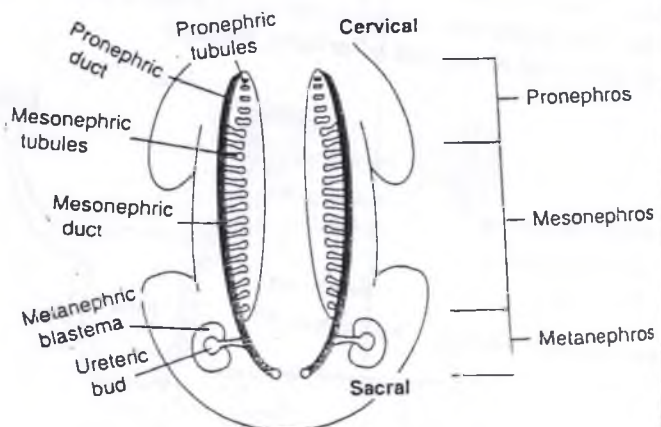
The human kidneys develop from the intermediate cell mass of mesoderm (nephrogenic cord)

Its development passes in 3 phases:

A. Pronephros, B. Mesonephros, C. Metanephros



Cross section in the embryo to show the intermediate cell mass of mesoderm



Front view of the embryo to show the pronephros, mesonephros and metanephros

Summary & Illustrations

Development of the kidney (continued)

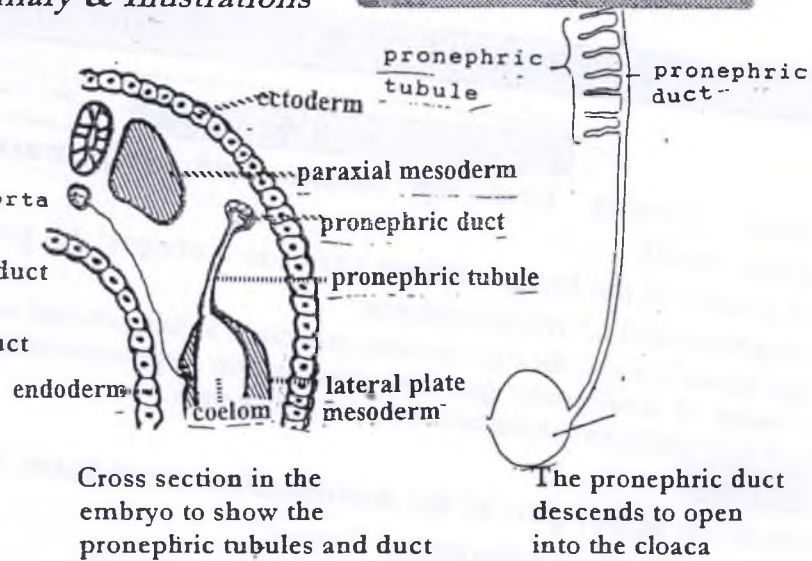
A. Pronephros

5 to 7 pronephric tubules appear in the upper part of the intermediate mesoderm. One end of the tube opens into the intra-embryonic coelom.

The other end opens into the pronephric duct.

By the 4th week, the tubules degenerate.

The pronephric duct → mesonephric duct.

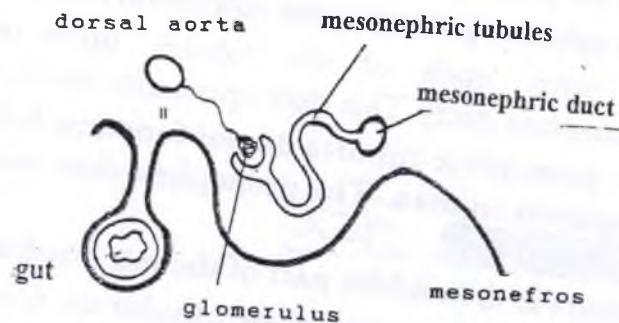


B. Mesonephros

70-80 S-shaped tubules appear in the middle part of the intermediate mesoderm.

The medial end of each tubule is invaginated by an artery of the dorsal aorta → forming the glomerulus.

The lateral end opens into the mesonephric duct.



Fate of mesonephros

In male

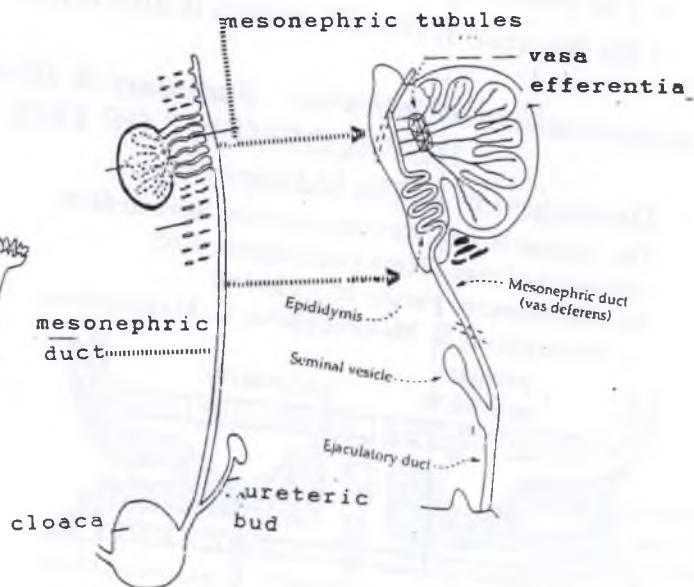
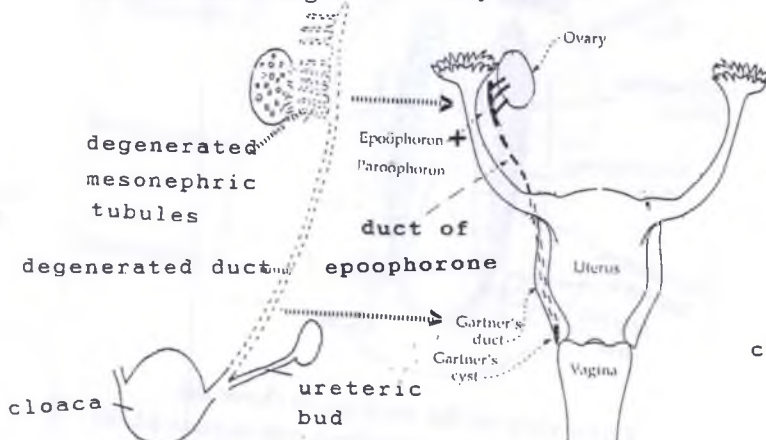
The tubules give vasa efferentia of the testis.

The duct gives epididymis, vas deferens, seminal vesicle, ejaculatory duct + ureteric bud + trigone of urinary bladder & part of prostatic urethra.

In female

The tubules mostly degenerate, however, few tubules may remain forming epoophorone, paroophorone (embryonic remnants in the mesovarium of the broad ligament).

The duct gives duct of epoophorone, Gartner's duct + ureteric bud & trigone of urinary bladder.



Derivatives of the mesonephric tubules and duct

Part	Derivatives in the male embryo	Derivatives in the female embryo
Mesonephric tubules	• The upper tubules degenerate • The middle, the lower tubules form the vasa efferentia (efferent ductules) of the testis, head of epididymis & paradydymis	Degenerate, few rudimentary tubules remain forming epoophoron + paraophoron (embryonic remnants in the mesovarium of the broad ligament)
Mesonephric duct	Forms the body, tail of epididymis, vas deferens, seminal vesicle & ejaculatory duct + ureteric bud & trigone of urinary bladder	Degenerates, part of the duct remains forming duct of epoophoron, Gartner's duct* + ureteric bud & trigone of urinary bladder.

* The Gartner's duct may swell to form **Gartner's cyst** which lies very close to the vagina.

C. Metanephros

The metanephros (or permanent kidney) develops from **2 sources**:

- i. **Ureteric bud**: which forms the **collecting part** of the kidney.
- ii. **Metanephric cap**: which forms the whole nephron (**excretory units** of kidney)

The ureteric bud:

It arises as a diverticulum from the lower end of the mesonephric duct (close to the cloaca). Its free end expands and comes in contact with the **metanephric cap** which lies in the pelvis.

Elongation of the ureteric bud will push the metanephric cap cranially (**ascent of the kidney**) to reach the level of the **upper lumbar segments** (adult position of kidney).

- **The cranial end of the ureteric bud** divides repeatedly to form i. **major calyces**, ii. **minor calyces** and iii. the **collecting tubules** of the kidney.

Each collecting tubule becomes covered by a separate small mass of mesoderm from the **metanephric cap**.

Metanephric cap:

- This is the **lower part of the intermediate column of mesoderm** after its segmentation into small masses.
- Each mass surrounds the distal end of the ureteric bud, forming what is called metanephric cap.
- The mesoderm of the **metanephric cap** differentiates into nephrons, i.e. it forms:
 - i) **Bowman's capsule**, ii) **proximal convoluted tubule**, iii) **loop of Henle**, &
 - iv) **distal convoluted tubule**.

The distal convoluted tubules join the collecting tubules to form complete uriniferous tubules.

Summary & Illustrations

Development of the kidney (continued)

C. Metanephros

The metanephros or permanent kidney develops from 2 sources:

i. Ureteric bud, ii. Metanephric cap.

i. Ureteric bud:

Arises from the lower end of the mesonephric duct

It gives the collecting part of the kidney:

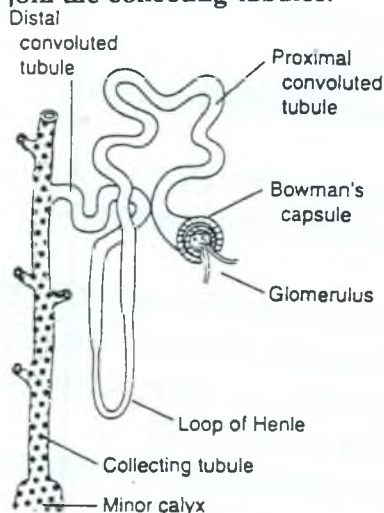
Ureter, pelvis of the kidney, major calyces, minor calyces and collecting tubules.

ii. Metanephric cap:

it is the lower segments of the intermediate mesoderm.

It is segmented into small masses.

Each mass gives the nephron (excretory unit of the kidney): **Bowman's capsule**, **proximal convoluted tubule**, **loop of Henle** and **distal convoluted tubules** which join the collecting tubules.



Derivatives of the metanephric cap

Ascent, rotation & changes in the shape and blood supply of the kidneys

In the early stages, the kidneys lie in the pelvis

Later, they migrate upwards to the abdomen

In the early stages, the convex border of each kidney is directed backwards and the hilum forwards

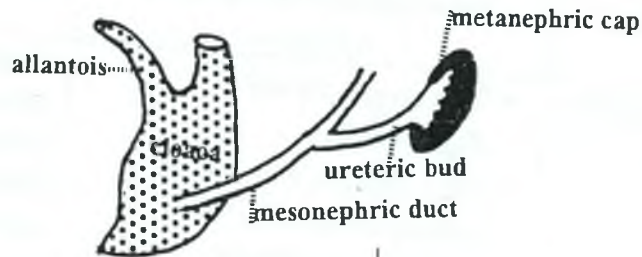
Later, the kidneys rotate 90° so the convex border becomes lateral and the hilum becomes medial.

In the early stages, the kidney is lobulated

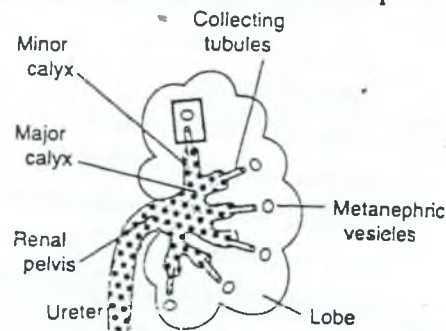
later, its surface becomes smooth

In the early stages, they receive blood supply from pelvic vessels (median sacral, common iliac arteries)

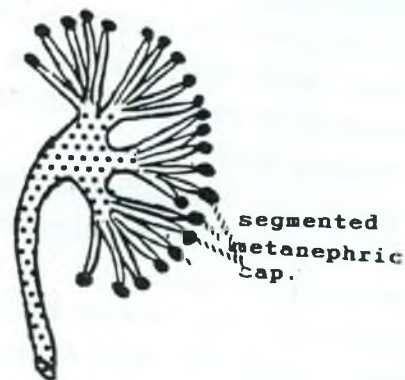
Later, they ascend and receive arteries from abdominal vessels (abdominal aorta)



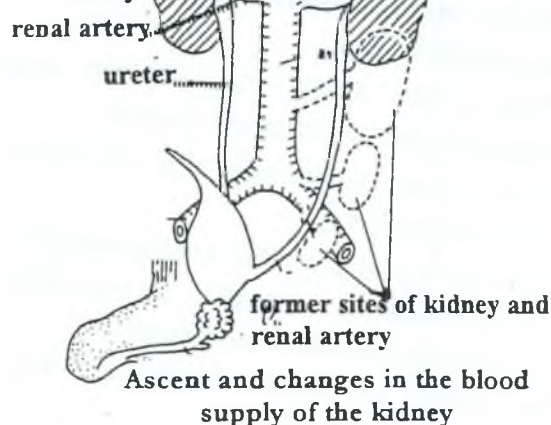
Metanephros = ureteric bud + metanephric cap



Derivatives of the ureteric bud

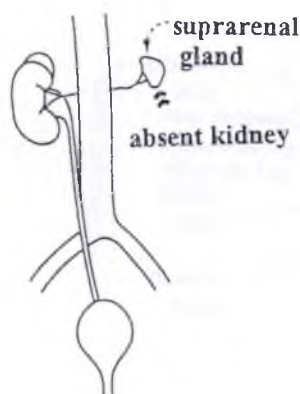


Segmentation of the metanephric cap kidney

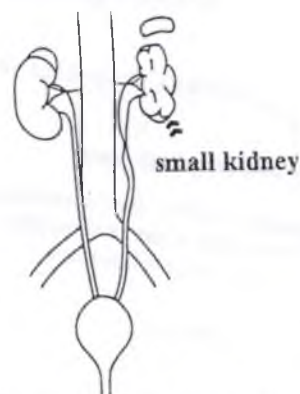


Summary & Illustrations

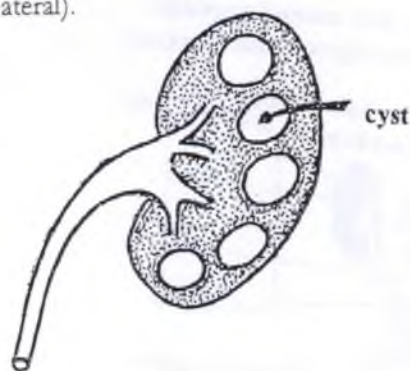
Commonest anomalies of the kidney



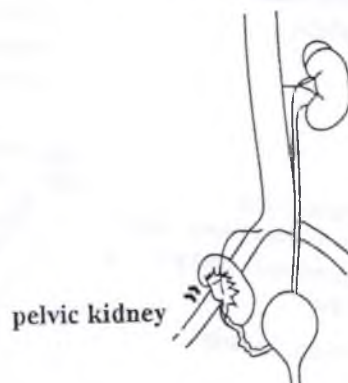
Renal agenesis: failure of the development of the kidney (unilateral or bilateral).



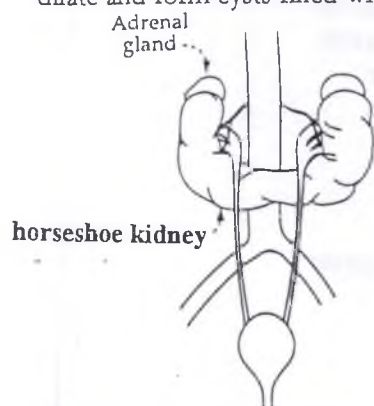
Renal hypogenesis: abnormally small-sized kidney.



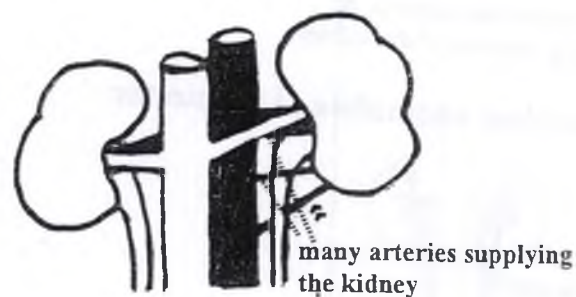
Congenital polycystic kidney: a congenital anomaly in which there is a failure of fusion between the excretory units (nephrons) and the collecting tubules. **Effect:** urine collects in the nephrons which dilate and form cysts filled with urine.



Pelvic kidney: the kidney retains its initial fetal position in the pelvis due to arrest of its normal ascent.

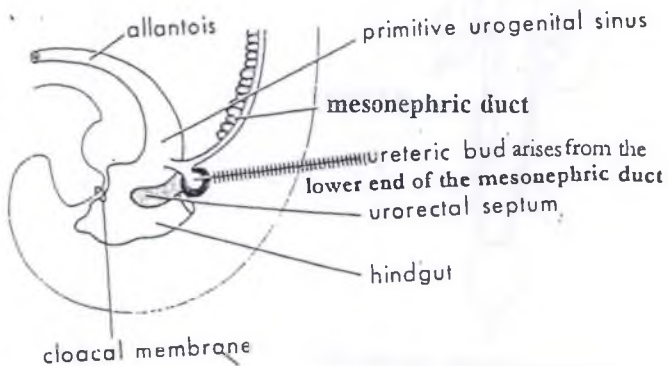


Horse shoe-shaped kidney: this is due to fusion of the lower poles of the 2 kidneys during their ascent from the pelvis to the abdomen.

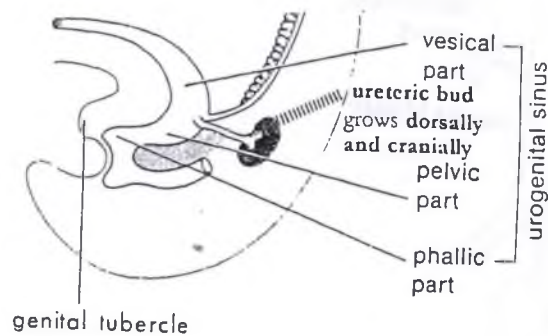


Aberrant renal vessels: these are additional branches of the aorta supplying the kidney.

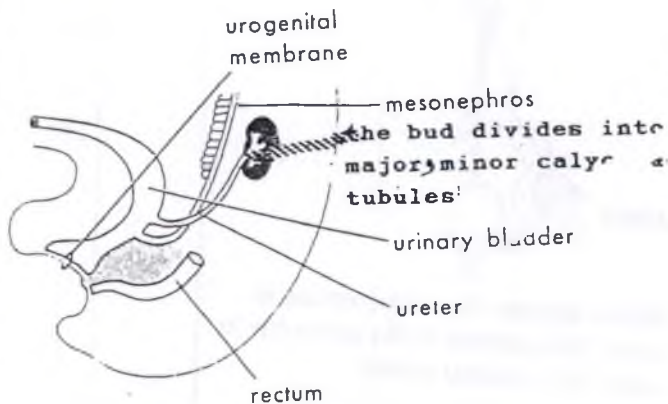
Summary & Illustrations Development of the Ureter



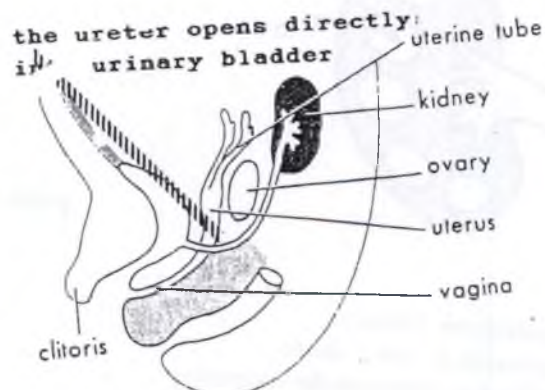
i. The ureter arises as a **hollow ureteric bud** from the **lower end of the mesonephric duct** close to the cloaca.



ii. It grows **dorsally and cranially** to come in contact with the **metanephric cap** of mesoderm, and **ascend together** to the of the lumbar region (adult position).

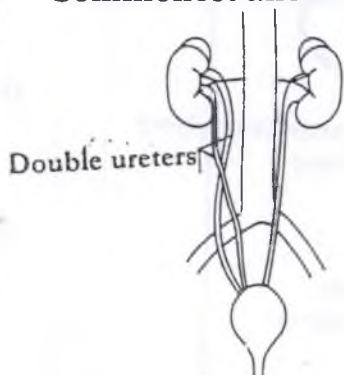


iii. Its upper end expands and divides repeatedly to form: **Pelvis of ureter, Major and minor calyces, & Collecting tubules** of the kidney.

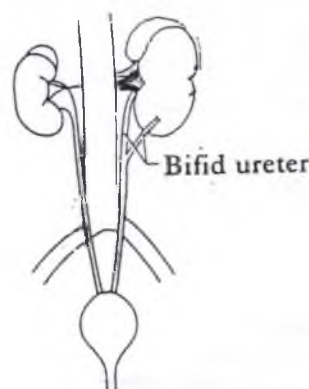


iv. By **absorption** of the caudal part of the mesonephric duct into the wall of the urogenital sinus, the ureter comes to **open directly into the urinary bladder**.

Commonest anomalies of the ureter:



1. **Double ureters:** 2 ureteric buds may develop from the mesonephric duct on one side.



2. **Bifid ureter or cleft pelvis of ureter:** Due to splitting of the upper end of the ureteric bud.

Development of Urinary Bladder

- The cloaca is the expanded distal part of the hindgut (endoderm).
- It is divided by the urorectal septum of mesoderm into ventral and dorsal parts.
- The ventral part is called the **primitive urogenital sinus**. This sinus receives the openings of the **allantoenteric diverticulum** and **two mesonephric ducts**.

The **primitive urogenital sinus** is divided by a constriction into two parts:

Upper part: **vesicourethral canal** which receives the allantoenteric diverticulum and 2 mesonephric ducts.

Lower part: **definitive urogenital sinus**.

The urinary bladder develops from 3 parts:

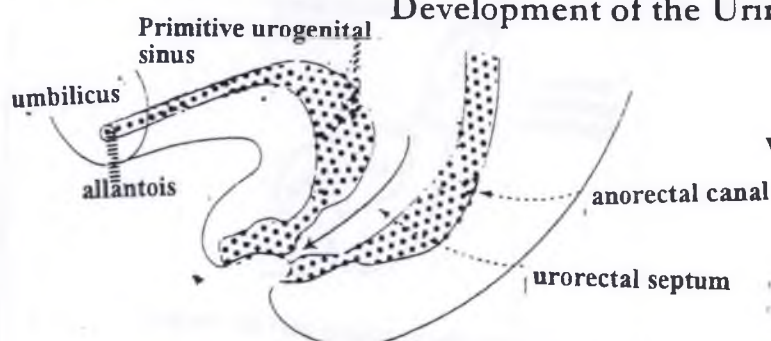
- A. **Vesicourethral canal (endoderm):** which forms the major part of the bladder.
- B. **Proximal part of allantois or allantoenteric diverticulum (endoderm):** which forms the **apex of the bladder**. The distal part of the diverticulum is called **urachus**. It is obliterated and forms the **median umbilical ligament**.
- C. **Proximal parts of the mesonephric ducts (mesoderm):** These are **absorbed** into the wall of the bladder to **form the trigone**.
 - By absorption of this part of the duct into the wall of the bladder, the ureter is now freed from the mesonephric ducts and opens directly into the urinary bladder.

Commonest anomalies:

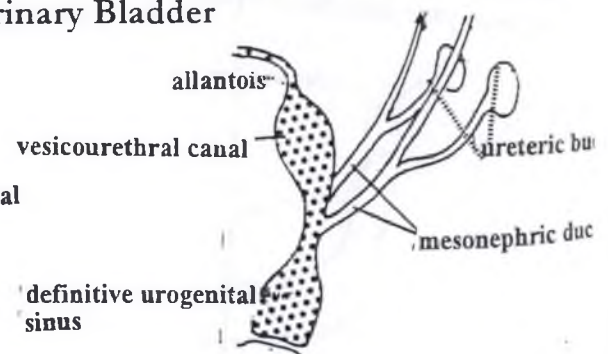
1. **Ectopia vesicae:** Failure of formation of the anterior wall of the bladder together with the infra-umbilical part of the anterior abdominal wall leads to opening of the bladder cavity into the surface just **above the symphysis pubis**. This anomaly is due to i. failure of formation of lower part of anterior abdominal wall. ii. Failure of formation of anterior wall of urinary bladder.
2. **Urachal fistula:** Due to failure of obliteration of the urachus after birth leading to dribbling of urine from the umbilicus.
3. **Urachal cyst:** Non obliteration of a localized part of the urachus leading to formation of a cyst.
4. **Urachal sinus:** The proximal part of the urachus is fibrosed, while its distal part remains patent leading to the formation of sinus.

Summary & Illustrations

Development of the Urinary Bladder



- i. Mesodermal urorectal septum divides the **cloaca** into ventral **primitive urogenital sinus** and dorsal **anorectal canal**



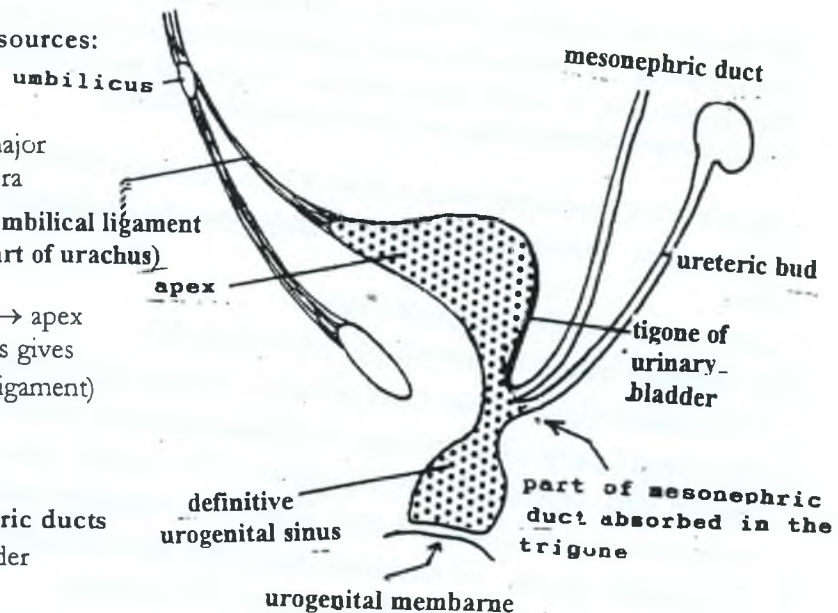
- ii. The primitive urogenital sinus is divided into vesicourethral canal & definitive urogenital sinus. The vesicourethral canal receives the **allantois** and 2 mesonephric ducts

Summary & Illustrations

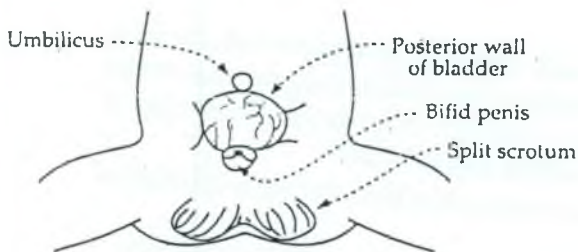
Development of the urinary bladder (continued)

The urinary bladder is developed from 3 sources:

- i. **Vesicourethral canal (endoderm)** → major parts of the urinary bladder & prostatic urethra
- ii. **Proximal part of allantois (endoderm)** → apex urinary bladder (the distal part of the allantois gives urachus → obliterated → median umbilical ligament)
- iii. **Absorbed proximal parts of mesonephric ducts (mesoderm)** → the trigone of urinary bladder

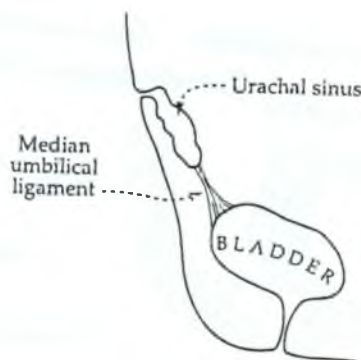


Commonest anomalies



1. **Ectopia vesica:** The bladder opens directly on the surface of the lower abdomen. It is usually accompanied by other anomalies, i.e. bifid penis and split scrotum

2. **Urachal fistula:** failure of obliteration of urachus (dribbling of urine from the umbilicus)



3. **Urachal cyst:** non obliteration of localized part of urachus.

4. **Urachal sinus:** the proximal part of urachus is fibrosed while the distal part is patent forming a sinus

Development of male urethra

The male urethra is divided into 3 parts: **Prostatic, Membranous & Spongy**.

They are derived from:

- **The upper part of prostatic urethra:** (above the openings of the ejaculatory ducts). It is derived from 2 sources:
 - i. Lower (caudal) part of the **vesico-urethral canal** (endoderm).
 - ii. Absorbed parts of the **mesonephric ducts** (mesoderm) form the posterior wall of this part of the urethra.
- **The Lower part of prostatic urethra** (below the openings of the ejaculatory ducts) and the **membranous urethra** are derived from the pelvic (upper) part of the **definitive urogenital sinus** (endoderm).
- **The Spongy urethra** is derived mainly from: i. the **endodermal phallic** (lower) part of the urogenital sinus as well as ii. the migrating **ectodermal** cells from the tip of glans phallus (penis).

The development of the spongy urethra passes as follows:

- The endodermal cells of the phallic part of urogenital sinus form a process called the **urethral plate**.
- The urethral plate extends on the **under surface (ventral surface)** of the **phallus** (primitive penis) as far as the glans phallus only.
- The plate shows a **longitudinal groove** called **urethral groove**.
- The edges of this groove are called **urethral folds (genital folds)**.
- The 2 urethral folds fuse in the median plane from behind forwards to form the **urethral canal** (endodermal).
- The urethral canal **opens posteriorly** into the pelvic part of the urogenital sinus. Anteriorly, the canal stops at the glans phallus.
- A **cord of ectodermal** cells grows from the **tip of the glans** and extends **backwards** till it meets the anterior end of the urethral canal. This cord is **canalized**, the two parts of the penile urethra become continuous with each other.

Anomalies

1. **Hypospadias:** It is **failure of fusion of the edges of the urethral groove** on the under surface of the penis. The urethra comes to open on the under surface of the penis, instead of at its tip.
2. **Epispadias:** The urethra opens on the **dorsum** of the penis. This is due to development of the glans penis (genital tubercle) in an **abnormally lower position**. In this case the penile urethra will develop on the dorsal surface of the penis instead of the under surface.
3. **Urethral stenosis (stricture):** It is narrowing of the urethral canal due to **incomplete canalization**.

NB. **Development of the prostate gland:** It develops as multiple (15-20) outgrowths (buds) from the lining of the prostatic urethra which become canalized to form the alveoli & ducts of the gland. The connective tissue & capsule are derived from surrounding mesoderm.

Development of the female urethra

The whole female urethra is developed with the urinary bladder from the endoderm of the vesicourethral canal of the cloaca.

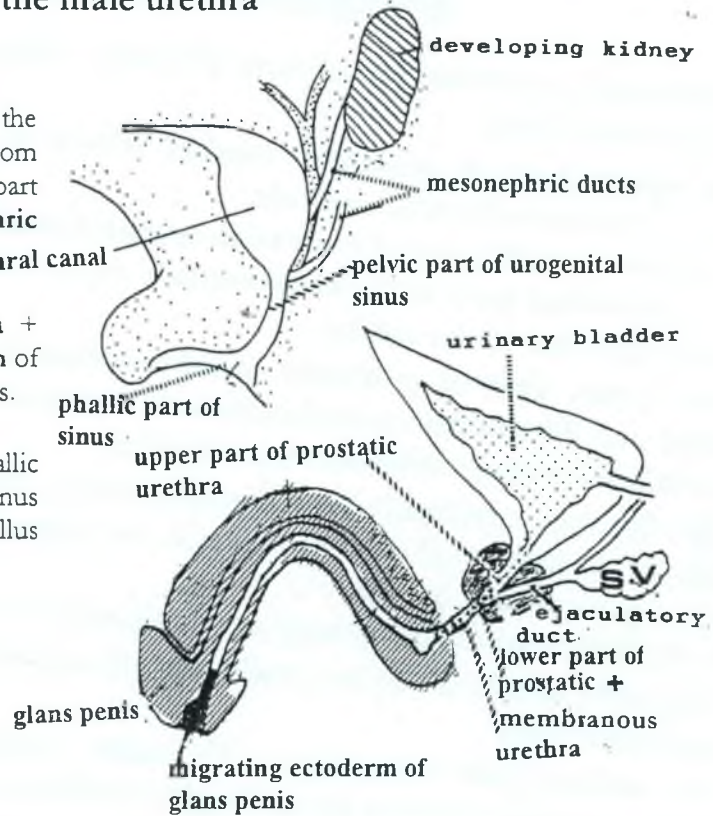
Summary & Illustrations

Development of the male urethra

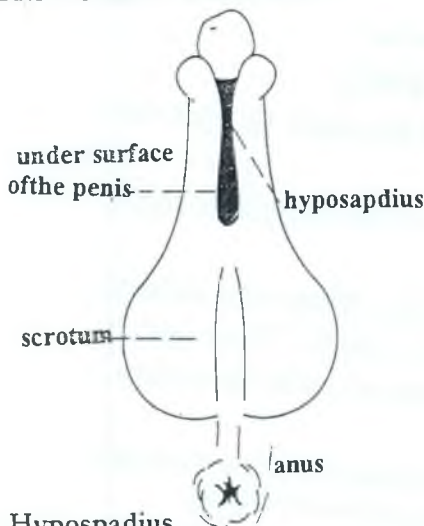
• The upper part of the prostatic urethra (till the opening of the ejaculatory duct) derives from **endoderm** of the distal end of the vesicourethral part of the cloaca + absorbed part of the **mesonephric** duct.

• The lower part of the prostatic urethra + **membranous urethra** derives from the **endoderm** of the upper pelvic part of the definitive urogenital sinus.

• **Spongy (penile) urethra** derives from the phallic (distal) part of the definitive urogenital sinus (**endoderm**) + migrating **ectoderm** of the glans phallus (penis).

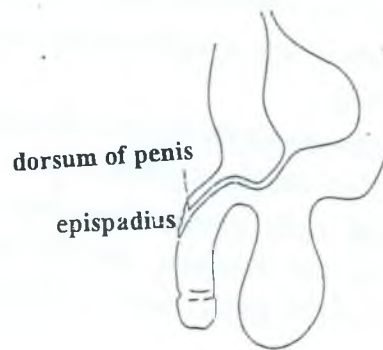


Commonest anomalies



1. Hypospadias

The urethra opens on the under surface of penis



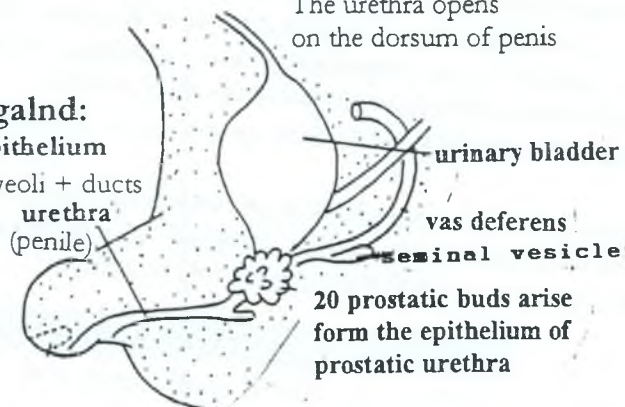
2. Epispadias

The urethra opens on the dorsum of penis

Development of the prostate gland:

15 to 12 prostatic buds arise from the **epithelium** of the **prostatic urethra** → gives the alveoli + ducts of the gland.

The **surrounding mesoderm** → gives the connective tissue and capsule.



DEVELOPMENT OF THE GENITAL SYSTEM

Development of the Gonads

Although the sex of the embryo is determined genetically at the time of fertilization, gonads do not acquire male or female morphologic characteristics until the 7th week. So the development of gonads passes in 2 stages:

1. Indifferent gonad (till the 7th week)
2. Stage of differentiation i.e. Development of testis or ovary (starts from the 7th week).

1 Indifferent Gonad

The primitive testis or ovary (indifferent Gonad) develops from 3 sources

- i. **Genital ridge:** It is the medial part of the mesonephros (intermediate cell mass of the mesoderm) which gives the fibrous capsule, stroma and connective tissue of the Gonad.
- ii. **The Coelomic epithelium** (mesoderm) covers the genital ridge: multiplies and forms the cells of the sex cords (Sertoli or follicular cells).
- iii. **The primordial germ cells (endodermal)** which migrate from the wall of the yolk sac through the dorsal mesentery to reach the genital ridge (at the 5th week).

At the 6th week the primordial germ cells invade the genital ridge to lie in between the cells of the sex cords and become spermatogonia in male or oogonia in female.

- N.B - At the beginning of the 7th week

- i) If the primordial germ cells carry "xy" sex chromosomes (due to the direct influence of the Y chromosome), the gonad will be differentiated to develop testis.
- ii) If the primordial germ cells carry "xx" sex chromosomes (due to the absence of the Y chromosome), the gonad will be differentiated to develop ovary.

2. Stage of differentiation

It means development of the testis or development of the ovary.

This stage includes i. the differentiation of the primordial germ cells into spermatogonia or oogonia. ii. Transformation of the sex cords into seminiferous tubules in the testis or primary follicles in the ovary. iii. Descent of the testis into the scrotum or descent of the ovary in the pelvis.

* In the following paragraphs, and in order to give a full picture about the development of the testis or the ovary, all the stages (including the indifferent stage) will be described, as well as the commonest anomalies.

Summary & Illustrations

DEVELOPMENT OF THE GENITAL SYSTEM

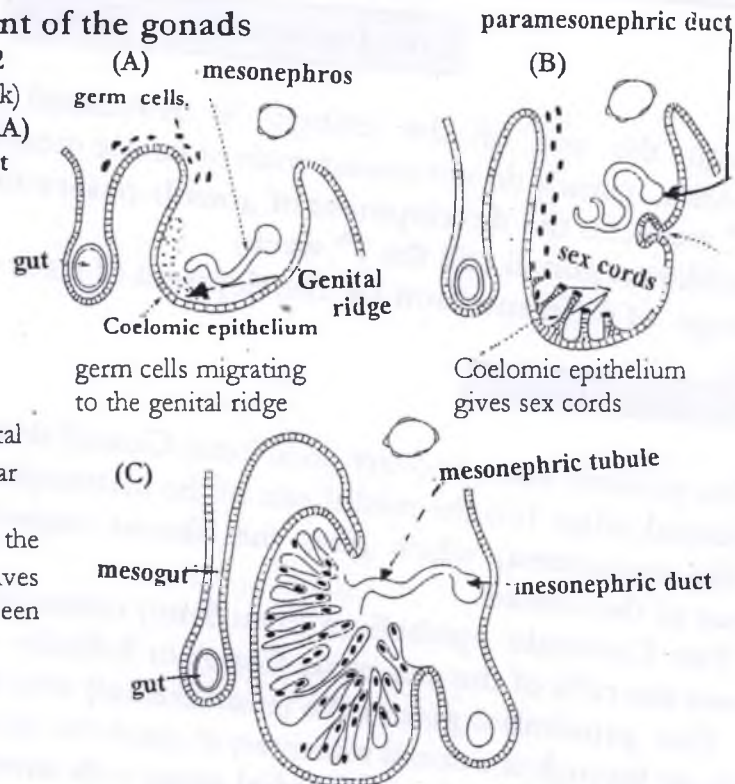
Development of the gonads

The development of the testis or ovary passes in 2 stages: 1. **indifferent gonads** (before the 7th week) & 2. **Stage of differentiation** which includes (2A) development of the testis or (2B) development of the ovary (starts from the 7th week).

1. Indifferent gonads

Each of the testis or ovary develops from:

- i. **Genital ridge**: it is the medial part of the mesonephros → it gives capsule, stroma & connective tissue of the gonad.
- ii. **Coelomic epithelium**, which covers the genital ridge → gives the sex cords (Sertoli or follicular cells).
- iii. **Primordial germ cells**, which migrate from the wall of the yolk sac → which gives spermatogonia or oogonia which lie in between the cells of the sex cords.



Germ cells lie in between the cell of the sex cords

Development of Testis

The testis develops from 3 sources:

1- **Genital ridge**: It is the medial part of the mesonephros. It forms the connective tissue of the testis and its covering **tunica albuginea**.

2- **The coelomic epithelium** (mesoderm): Gives rise to the cells (Sertoli) of the sex (testis) cords.

3- **The primordial germ cells**: These are **endodermal** cells that migrate from the caudal wall of the yolk sac and give rise to **spermatogonia**.

- The primitive **sex cords**, branch, anastomose forming **testis cords**.
- The germ cells (**spermatogonia**) become incorporated in the testis cords.
- The testis cords lose their connection with the surface epithelium and canalize to form the **seminiferous tubules**.
- The seminiferous tubules are horse shoe-shaped with straight ends, called **straight tubules**.
- The **straight tubules** anastomose together at the hilum of the testis forming **rete testis**.
- The rete testis becomes connected to the epididymis (mesonephric duct) by means of the **vasa efferentia** (mesonephric tubules).

Descent of the testis:

The testis develops at the level of the first lumbar segment. It undergoes **internal descent** to reach the deep inguinal ring. Then, it undergoes **external descent** through the inguinal canal to reach the scrotum.

-In the **seventh month** of fetal life it lies in the **deep inguinal ring**.

-In the **eighth month** it transverse the **inguinal canal**.

-In **ninth month** it lies near the **superficial ring**.

-It reaches the **scrotum** before birth.

NB. 1. The testis develops as an abdominal organ, then it migrates into the scrotum, dragging with it the testicular artery which arises from the abdominal aorta.

2. The peritoneum of the coelomic cavity in the abdomen sends an invagination follow the course of the testis into the scrotum and is known as processus vaginalis.

3. The processus vaginalis forms a covering for the testis in the scrotum formed of 2 layers (parietal, visceral).

4. The narrow canal which connects the processus vaginal with the peritoneal cavity is obliterated just before birth.

Causes of descent:

i) Elongation of the upper half of the body leading to a relative caudal shift in the position of the testis (**internal descent**).

ii) Contraction of the **gubernaculum** (not accepted).

The gubernaculum is a fibrocellular cord which connects the testis with the scrotum. Shortness of this cord causes of the testis.

iii) Normal herniation helped by the **increased intra-abdominal pressure**.

Commonest anomalies

1-Cryptorchism: failure of descent of the testis (undescended testis). The testis may be in the abdomen, in the inguinal canal or in the superficial inguinal ring.

2-Maldescended testis: descent of the testis to an abnormal position e.g. perineum, root of the penis or the femoral triangle.

3-Congenital inguinal hernia: some of the abdominal contents pass to the scrotum. This is due to failure of obliteration of the processus vaginalis.

Development of the ovary

The ovary develops from 3 sources:

1- **Genital ridge:** It is the medial part of the mesonephros. It forms the **stroma**, connective tissue of the ovary and its covering **tunica albuginea**.

2- **Coelomic epithelium (mesoderm):** Gives rise to cells of sex cords (follicular cells).

3- **Primordial germ cells:** These are **endodermal cells** that migrate from the wall of the yolk sac and give rise to **oogonia**.

-The germ cells (oogonia) become incorporated in the sex cords.

The **sex cords** become divided into separate masses termed **primary (primordial) follicles**.

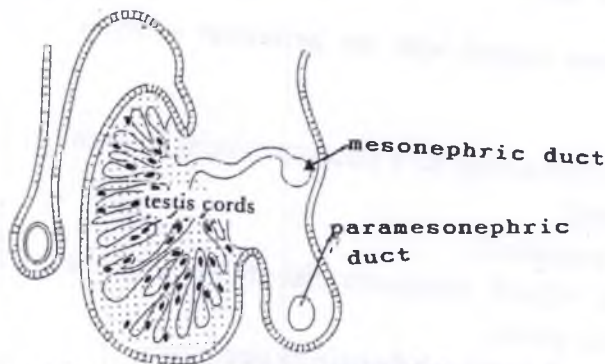
Each follicle is formed of an oogonium surrounded by a single layer of follicular cells.

Summary & Illustrations

2A. Development of the testis:

It is developed from 3 sources:

- i. **Genital ridge:** It is the medial side of the mesonephros → gives the **capsule** (tunica albuginea), connective tissue **stroma** and **septa** of the testis.
- ii. **Coelomic epithelium** (mesoderm) which covers the genital ridge → gives the **testis cords** → **seminiferous tubules** and **rete testis**.
- iii. **Primordial germ cells** (endoderm) migrating from the wall of the yolk sac → gives **spermatogonia** which lie in between the cells of the sex cords.



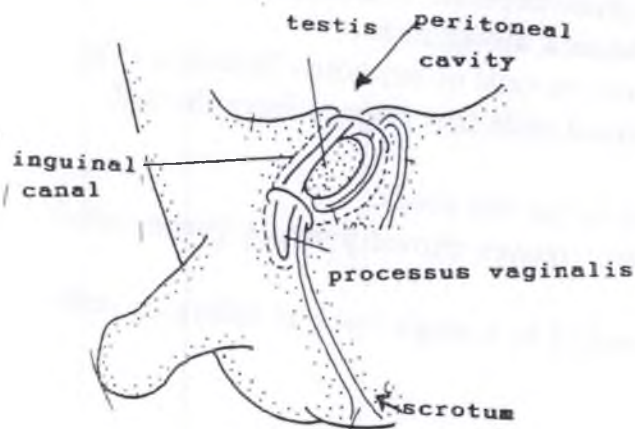
Germ cells (spermatogonia) intermingled in between the cells of testis cords

Descent of the testis:

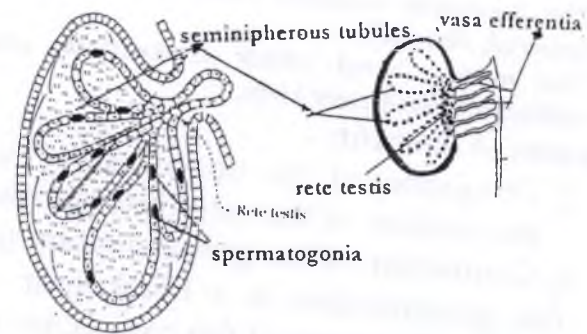
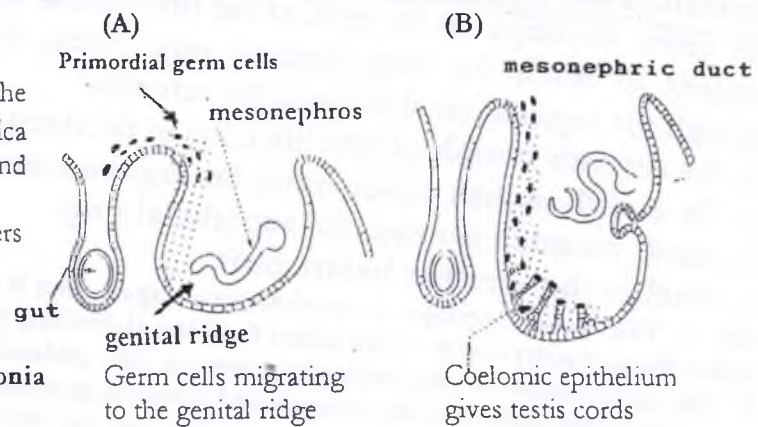
- It develops in the abdomen then descends reaching the **deep inguinal ring** (internal descent) at the 7th month.
- It migrates in the **inguinal canal** at the 8th month.
- It reaches the scrotum just before birth.

Causes of descent:

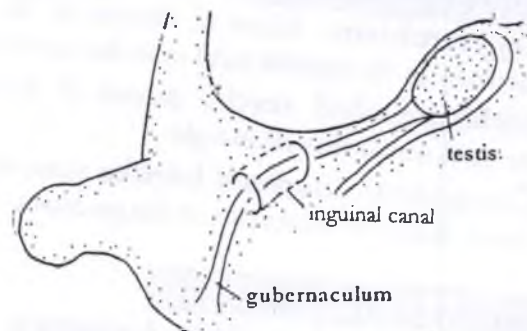
1. Internal descent
2. Rise of intra-abdominal pressure
3. Shortness of gubernaculum.



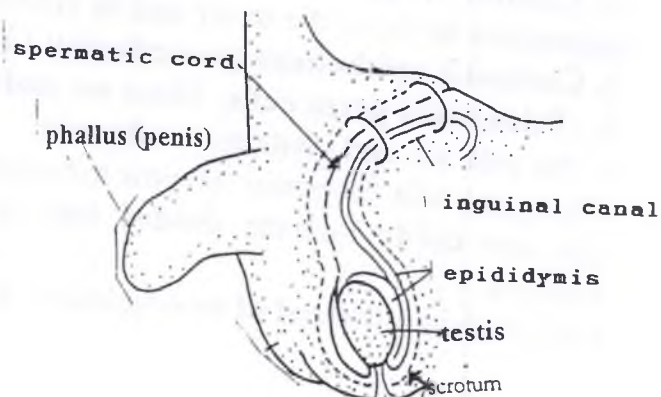
At the 8th month, the testis migrates through the inguinal canal



The testis cords become **seminiferous tubules**. Their straight ends become **rete testis** which joins the mesonephric tubules (**vasa efferentia**).



Early in development, the testis lies in the abdomen. The **gubernaculum** connects it to the scrotum.



Just before birth, the testis lies in the scrotum

Development of the ovary (continued)

Descent of the ovary:

- The ovary is attached by **gubernaculum** which connects it to the **labium majus**.
- The ovary develops opposite the first lumbar segment. Then, it undergoes **internal descent** to lie in the pelvis. More descent is arrested due to attachment of the gubernaculum to the side of the uterus.
- The part of **gubernaculum** between the ovary and uterus form the **ligament of the ovary**. The part between the uterus and labium majus form the **round ligament of the uterus**.

Commonest anomalies

1. **Ovarian agenesis**: Congenital absence of the ovary → Turner syndrome
2. **Imperfect descent**: The ovary fails to descend to pelvis or may be pulled to inguinal canal.

Paramesonephric (Mullerian) Ducts

- It is a longitudinal duct (one on each side) that descends very close to the mesonephros and its mesonephric duct. The paramesonephric ducts arise as 2 longitudinal invaginations of the coelomic epithelium lateral to the mesonephric ducts. These ducts are well developed in females and will be differentiated as follows:
- Each duct has 3 parts (upper vertical, middle horizontal and lower vertical)
- Their upper vertical parts and middle horizontal parts form the uterine tubes.
- Their lower vertical parts fuse together to form the utero-vaginal canal which has a solid lower tip. This solid lower tip grows downward and protrudes into the posterior wall of the urogenital sinus forming an elevation known as **Mullerian tubercle** which lies between the openings of the mesonephric ducts. This Mullerian tubercle induces 2 endodermal outgrowths (sinovaginal bulbs) from the urogenital sinus extending into the uterovaginal canal. The 2 sinovaginal bulbs unite to form the **vaginal plate** which grows upwards and canalizes to form the lower part of the vagina.
- The upper part of the utero-vaginal canal forms the uterus; while its lower part forms the upper part of the vagina.

N.B:

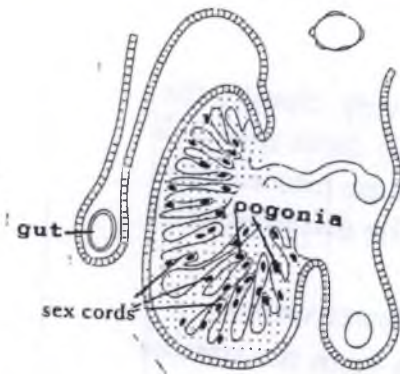
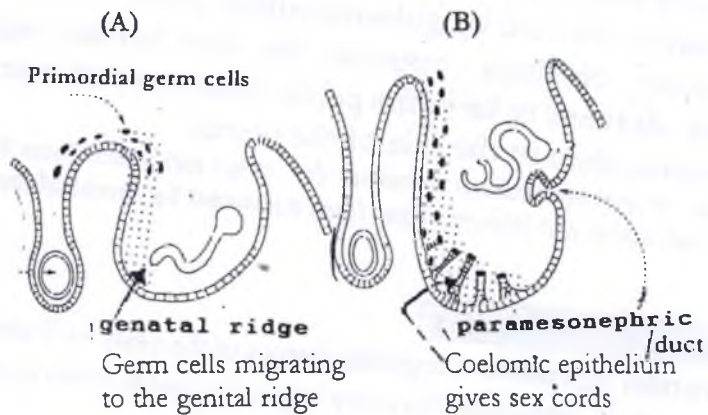
1. The lower part of the vagina is developed from the endoderm of the **vaginal plate**.
2. The vestibule of the vagina is developed from the endoderm of the **definitive urogenital sinus** of the cloaca.
3. The **hymen** is an incomplete septum separating the vestibule of the vagina from the vaginal canal. It is formed of A) epithelial lining of the vaginal canal. B) epithelial lining of the vestibule of the vagina.
4. **In the male**: the paramesonephric duct **disappears almost completely**, except for 2 small parts at its ends:
 - i- **Cranial end**: forms the **appendix of testis**.
 - ii- **Caudal end**: forms the **prostatic utricle**.

Summary & Illustrations

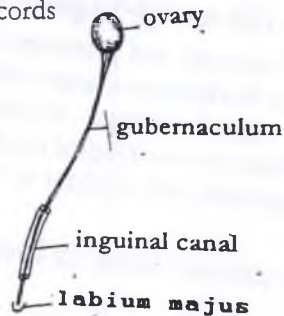
Development of the ovary

The ovary develops from 3 sources:

- Genital ridge** (medial part of mesonephros) → it gives **capsule** (tunica albuginea), connective tissue and **stroma** of the ovary.
 - coelomic epithelium** (mesoderm), which covers the genital ridge → gives **sex cords** (follicular cells)
 - Primordial germ cells** (endoderm) migrating from the wall of the yolk sac → gives **oogonia** which lie in between the cells of the sex cords.
- The sex cords divide into masses called **primary follicles**.



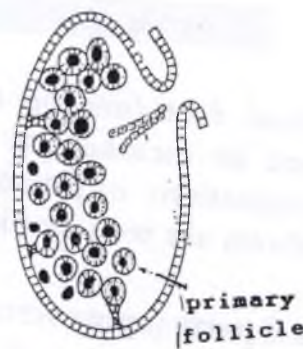
Germ cells (oogonia) intermingled in between the cells of the sex cords



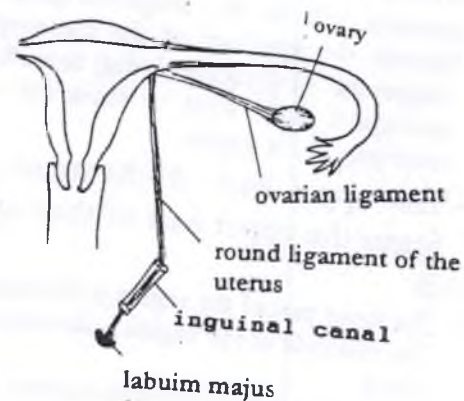
Early in development, the gubernaculum connects between the ovary and labium majus.

Descent of the ovary

The ovary develops in the abdomen. It undergoes internal descent to reach the pelvis. More descent is arrested due to attachment of the **gubernaculum** into the uterus. The **gubernaculum** becomes ovarian ligament + round ligament of the uterus.



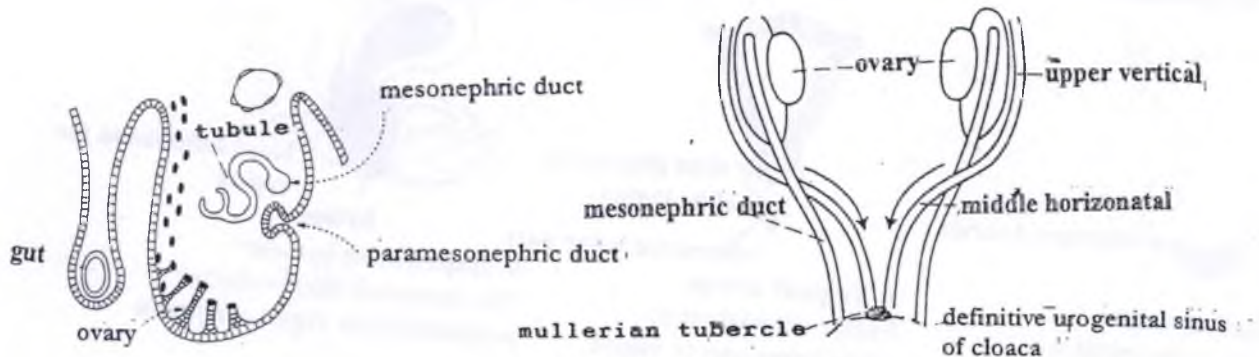
The sex cords become segmented into masses called primary follicles



In late pregnancy the gubernaculum becomes **ovarian ligament** and **round ligament of the ovary**

Summary & Illustrations

Paramesonephric (Mullerian) ducts

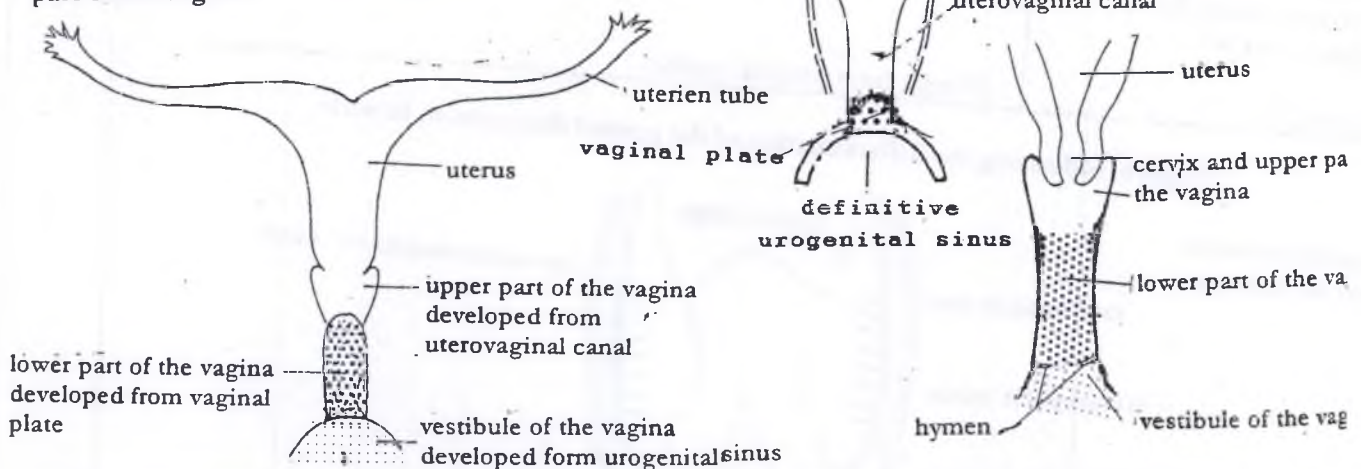


i. These are 2 longitudinal invaginations of the coelomic epithelium lateral to mesonephric ducts.

ii. Each duct has upper vertical, middle horizontal and lower vertical parts.

iii. -The upper vertical and middle horizontal parts form the uterine tubes.

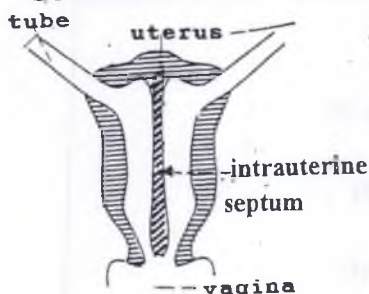
-The lower vertical parts fuse to form the utero-vaginal canal which gives the uterus and upper part of the vagina.



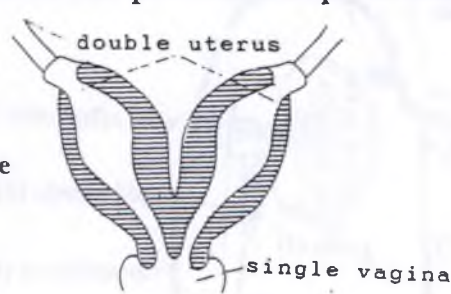
iv. -The lower part of the vagina is derived from the endoderm of the vaginal plate (sinovaginal bulb).

v. -The vestibule of the vagina is derived from the endoderm of the urogenital sinus of the cloaca. The **hymen** separates between the lower part of the vagina and vestibule

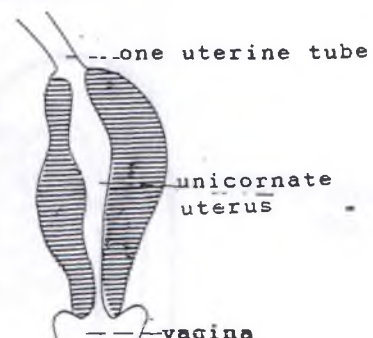
Commonest anomalies of the paramesonephric ducts



1. Persistence of the intrauterine septum



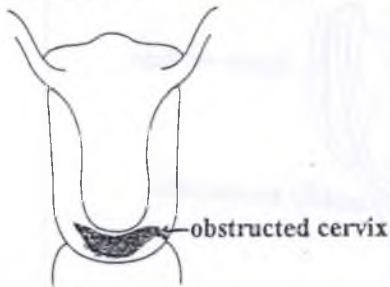
2. Double uterus & single vagina



3. Unicornate uterus
only one Mullerian duct developed

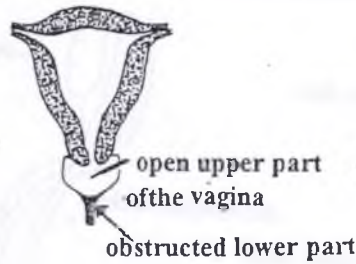
Summary & Illustrations

Commonest anomalies of the paramesonephric duct (continued)



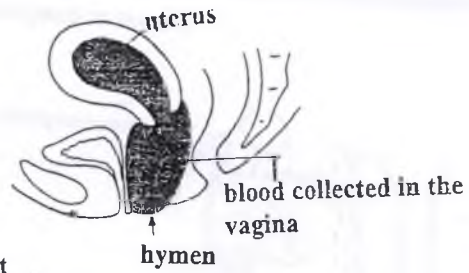
4. Cervical atresia

The cervix of the uterus is obstructed



5. Vaginal atresia

Failure of canalization of the lower part of vagina



6. Imperforate hymen

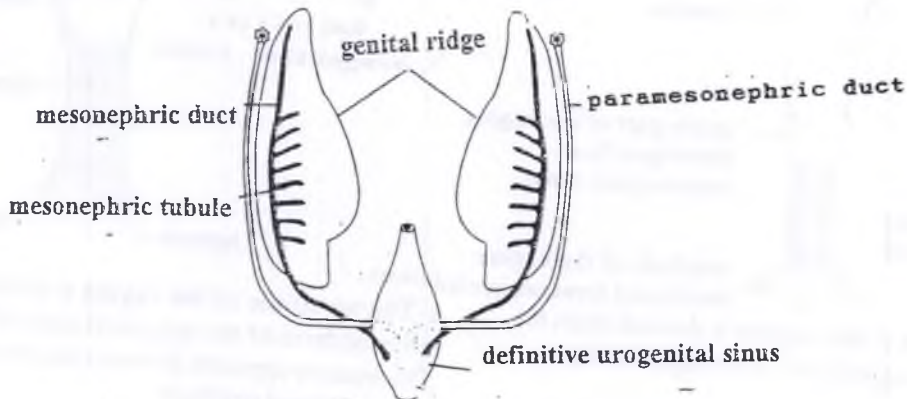
The menstrual blood collected progressively in vagina and uterus

Summary for the development of the genital system in male

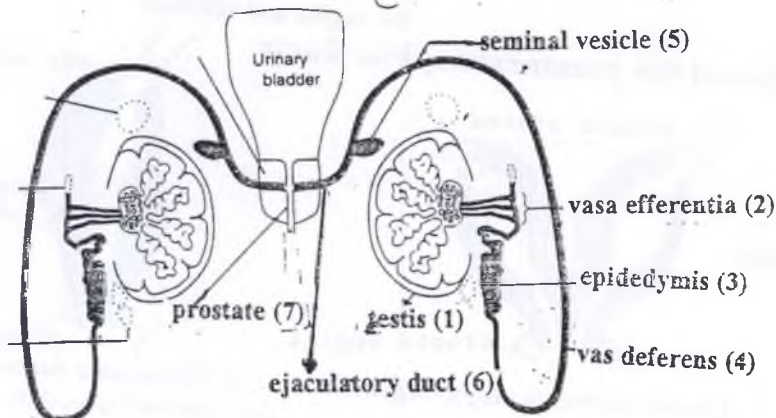
Organ	Derived from
- Testis (1)	- Genital ridge (medial part of mesonephros) + 1ry germ cells + coelomic epithelium
- Vasa efferentia (2)	- derive from mesonephric tubules
- epididymis (3), vas deferens (4), seminal vesicle (5), ejaculatory duct (6)	- 3-6 derive from mesonephric duct
- Prostate (7)	- 20 buds from prostatic urethra

Diagram indicating the differentiation of the genital duct system in male

A. genital system in the embryo



B. genital system at birth.



Summary & Illustrations

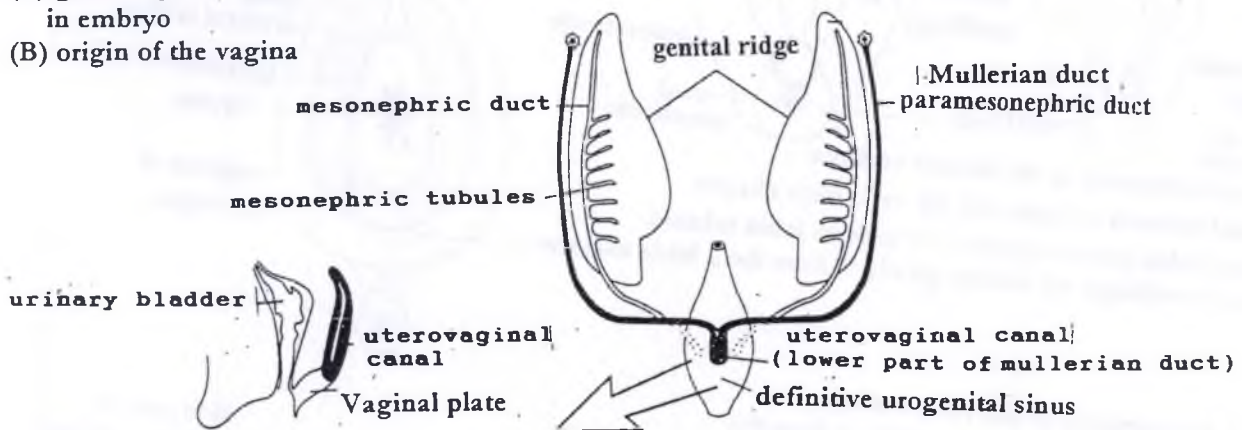
Summary for the development of the genital system in female

Organ	Derived from
-Ovary (1)	- Genital ridge (medial part of mesonephros) + 1ry germ cells + coelomic epithelium
-Uterine tube (2), uterus (3), upper part of the vagina (4).	- Mullerian duct (paramesonephric duct)
-Lower part of the vagina (5)	- Vaginal plate (sinovaginal bulb)
-Vestibule of the vagina (6)	-Endoderm of the definitive urogenital sinus

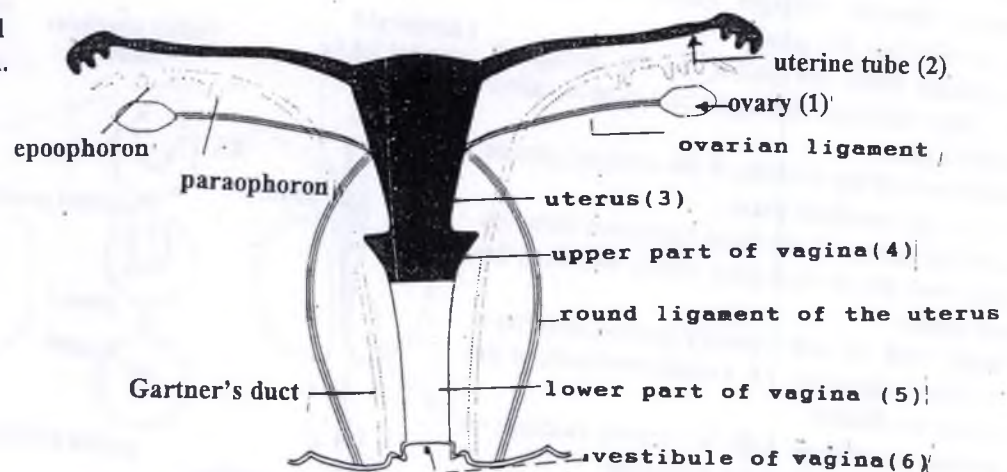
Diagram indicating the differentiation of the genital duct system in female

(A) genital system
in embryo

(B) origin of the vagina



(C) female genital
system at birth.



Development of the external genital organs

The development of external genital organs pass through 2 stages in both sexes:

1. Indifferent stage

2A. Further development in the female embryo, or 2B. Further development in the male embryo

1. Indifferent stage:

In the early stages, the external genital organs are identical in male and female. They appear as:

. Proliferation of the mesoderm in the cloacal region leads to appearance of 2 cloacal folds which surround the **cloacal membrane**.

B. More proliferation of the mesodermal cells and separation of the **cloacal membrane** into **urogenital and anal membranes** will lead to:

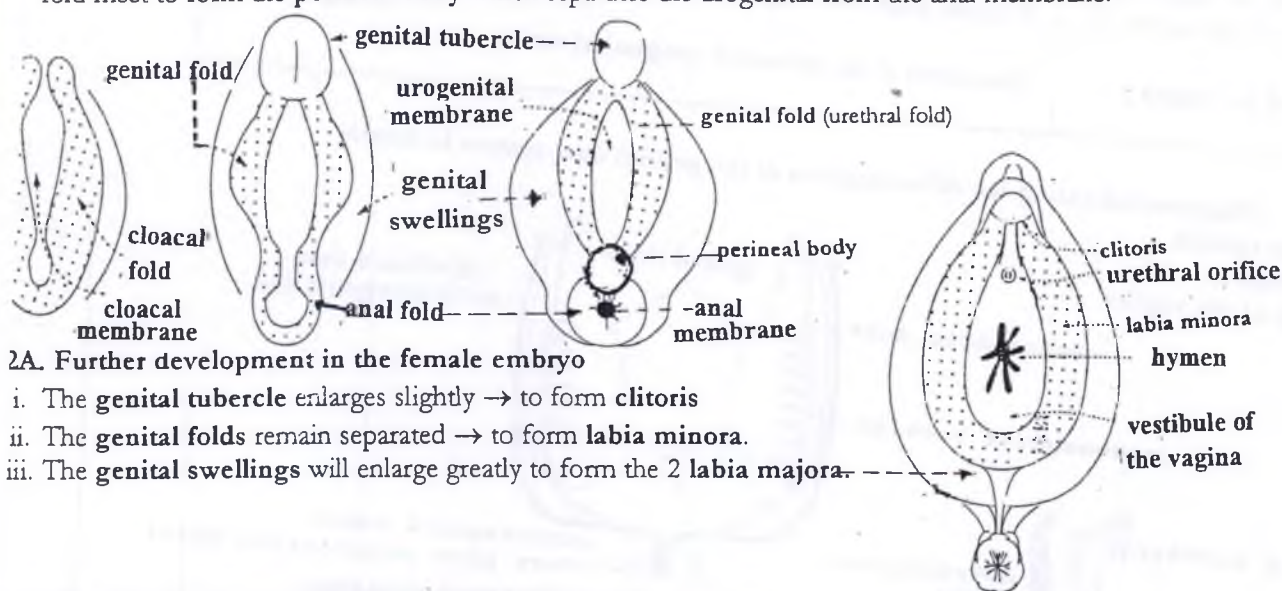
Summary & Illustrations

Development of the external genital organs (continued)

appearance of 2 **genital swellings** on either side of the cloacal folds (which now become the genital folds).

Division of the cloacal folds into rostral **genital fold** (urethral fold) which surrounds the **urogenital membrane** and caudal **anal fold** which surrounds anal membrane.

The anterior end of the genital folds meet to form **genital tubercle**. The posterior end of the genital fold meet to form the **perineal body** which separates the urogenital from the anal membrane.

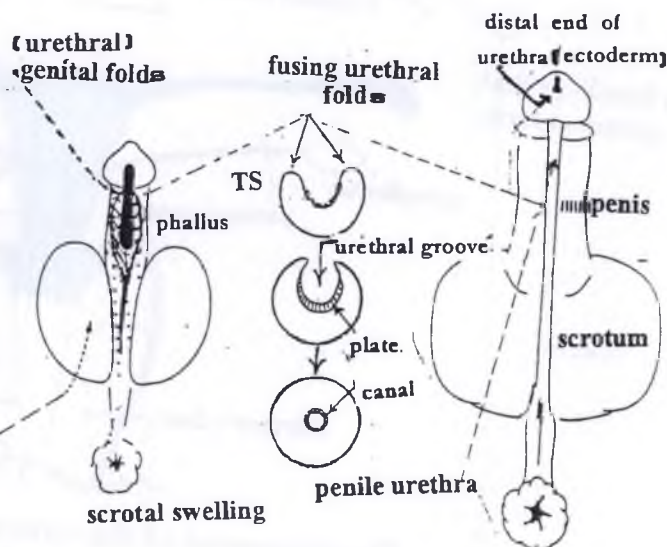


2A. Further development in the female embryo

- The **genital tubercle** enlarges slightly → to form **clitoris**
- The **genital folds** remain separated → to form **labia minora**.
- The **genital swellings** will enlarge greatly to form the 2 **labia majora**.

2B. Further development in the male embryo

- The **genital tubercle** enlarges greatly to form the **phallus** → will form the **penis**.
- The 2 **genital folds** are pulled by the elongated phallus. They will form the edges of a groove called the **urethral groove**.
- The endoderm of the bottom of the urethral groove → will form the **urethral plate**.
- Fusion of the urethral folds from backward forwards will close over the urethral plate which will form the **urethral canal**.
- The **distal end of the spongy (penile) urethra** is derived from migration of **ectodermal cells** at the tip of the glans phallus
- The **genital swellings** will be **scrotal swelling** → and will fuse together forming **scrotum**.



Commonest anomalies

- Hypospadias**: The external meatus is found on the undersurface of the penis. It is caused by failure of urethral folds to fuse together (page 45).
- Epispadias**: The external meatus is found in the upper (dorsal) surface of the penis (page 45).
- Pseudohermaphrodite**: The external genitalia belong to one sex while the gonads belong to the opposite sex.
- Male with small penis** due to under development of the genital tubercle.
- Female with large clitoris**: due to over development of the genital tubercle.
- Divided scrotum**: due to failure of fusion of the genital swellings in male.

DEVELOPMENT OF THE CARDIOVASCULAR SYSTEM

Development of The Heart

- The heart develops from the **cardiogenic area** of the **splanchnic mesoderm**, which lies **in front of the bucco-pharyngeal membrane**.
- During the 3rd week of intrauterine life, the heart is represented by a cells, which give rise to **2 endocardial heart tubes**.
- The tubes lie in the floor of the **pericardial cavity**.

After folding the tubes lie in the roof of the cavity

- The 2 endocardial heart tubes soon **unite together forming a single heart tube** which will form the **endocardium** of the heart.
- The **splanchnic mesoderm** surrounds the endocardial heart tube will differentiates into the **myocardium** & the **epicardium** of the heart.

The **pericardial cavity**: surrounds the heart tube which becomes suspended to the roof of the cavity by the dorsal mesocardium.

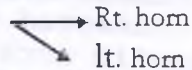
The **dorsal mesocardium** disappears later on leading to the formation of a passage dorsal to the heart tube called the **transverse sinus of the pericardium**.

The heart tube shows **5 dilatations** with constrictions in between:

- 1- **Sinus venosus** (most caudal).
- 2- **Common atrium**.
- 3- **Common ventricle**.
- 4- **Bulbus cordis**.
- 5- **Truncus arteriosus** (most cranial).

The heart tube changes its shape owing to its elongation. It becomes **U-shaped** and then **S-shaped**.

Fate of the 5 Heart dilatations

Embryonic Dilatation	Adult Structure
Sinus venosus 	-Smooth part of right atrium -Coronary sinus
Common atrium	-Rough part of right atrium (anterior wall + Rt. Auricle) -Rough part of left atrium (Lt. Auricle)
Common ventricle	-Rough part of right ventricle -Rough part of left ventricle
Bulbus cordis	-Smooth part of right ventricle (infundibulum) -Smooth part of left ventricle (vestibule)
Truncus arteriosus	-Ascending aorta -Pulmonary trunk

Summary & Illustrations

Development of the Cardiovascular System

Development Of the heart

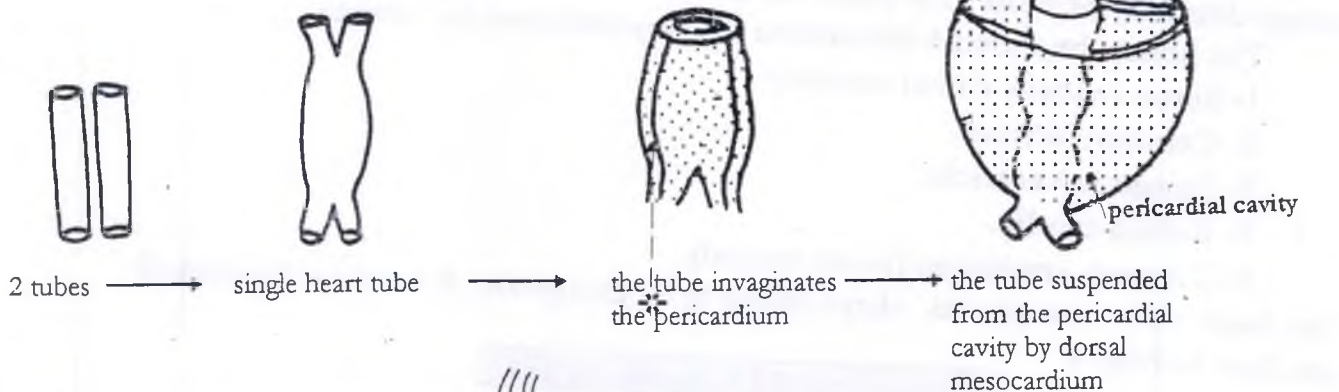
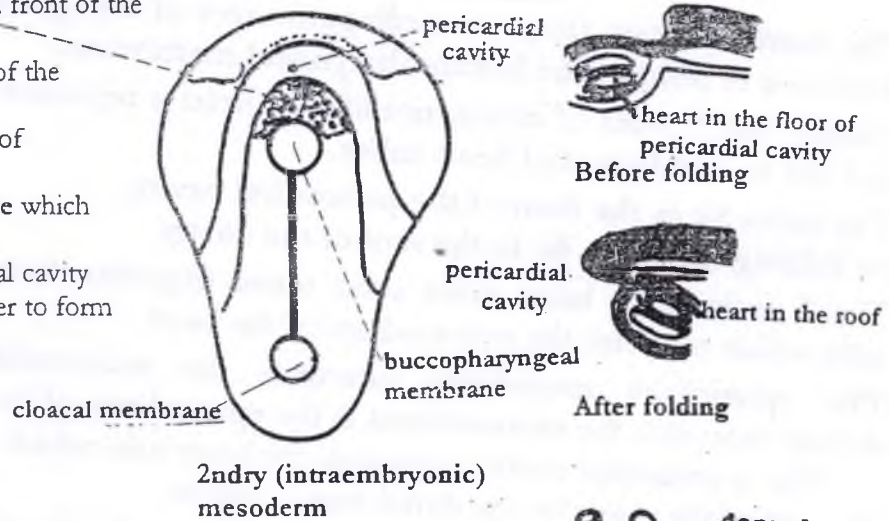
It is developed from the **mesoderm** in front of the buccopharyngeal membrane.

It appears as 2 heart tubes in the floor of the pericardial cavity.

After folding, the tubes lie in the **roof** of the cavity.

The 2 tubes unite to form single tube which invaginates the pericardial cavity.

The tube suspended from the pericardial cavity by **dorsal mesocardium** (absorbed later to form the **transverse sinus of pericardium**).



The heart tube shows 5 dilatations:

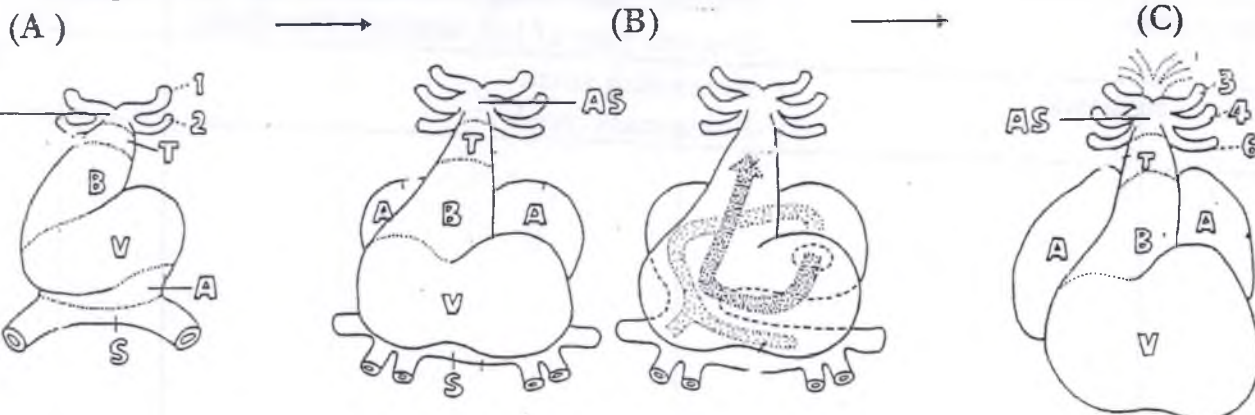
sinus venosus	S
Common atrium	A
common ventricle	V
Bulbus cordis	B
Truncus arteriosus	T



*** N.B :**
 *The aortic sac, is a dilatation at the upper end of the truncus arteriosus.
 *The aortic sac is connected to 6 pairs of arteries (Aortic arches).

AS: AORTIC SAC
1-6: AORTIC ARCHES

*** Changes in the shape of the heart tube:**



1. The sinus venosus

-The sinus venosus is the most caudal part of the heart tube & receives all the veins of the body of the fetus.

-It is formed of a small median part & 2 lateral horns : right & left.

-Each horn receives the following veins:

1- **Vitelline vein**: from the yolk sac.

2- **Umbilical vein**: from the placenta.

3- **Common Cardinal** (formed by the union of the anterior & posterior cardinal veins) from the body of the embryo itself.

The **sinus venosus** opens into the primitive atrium by a sino - atrial orifice guarded by right & left sinus venous valves.

Fate of the sinus venosus:

1- The right horn forms smooth posterior wall of the right atrium.

2- The left horn & body atrophy and form the coronary sinus.

3- The left common cardinal vein becomes the oblique vein of left atrium.

4- The right common cardinal vein forms the lower 1 / 2 of the superior vena cava.

5 The right sinus venous valve and the septum spurium (the fused upper part of right and left sinus venous valve) are transformed into:

- Crista terminalis of the right atrium, -Valve of inferior vena cava & -Valve of the coronary sinus.

6- The left sinus venous valve fuses with the interatrial septum.

Development of the atria

The development of the two atria passes in the following stages:

1- **Division of atrio-ventricular canal into 2 halves by septum intermedium:**

the atrioventricular canal becomes divided into right (tricuspid) & left (mitral) canals by the development of the **septum intermedium** (ventral, dorsal endocardial cushion).

2- **Division of the primitive common atrium into right & left halves by the development of the inter atrial septum.**

3- **Absorption of the Atrio-Ventricular Canals into the 2 atria:**

each of the right & the left atrio-ventricular canal becomes absorbed into the corresponding atrium.

4- **Absorption of the right horn of sinus venosus into the right atrium.**

5- **Absorption of the pulmonary veins into the left atrium.**

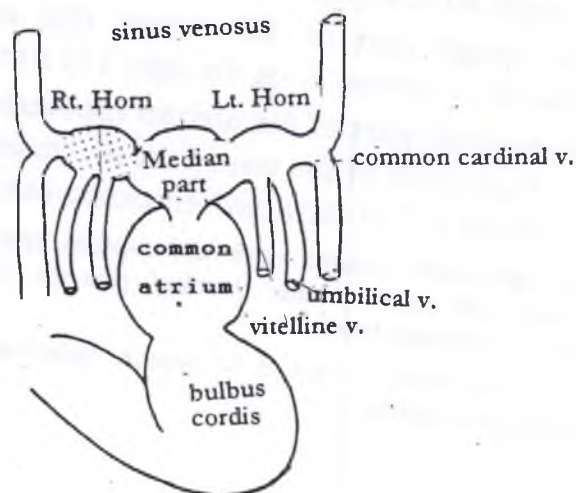
Summary & Illustrations

The Sinus Venosus

-Receives all veins of the fetus

-Formed of small median part (connected to the common atrium) + 2 horns (right and left)

-Each horn is connected to: i. Vitelline, ii. Umbilical & iii. Common cardinal veins

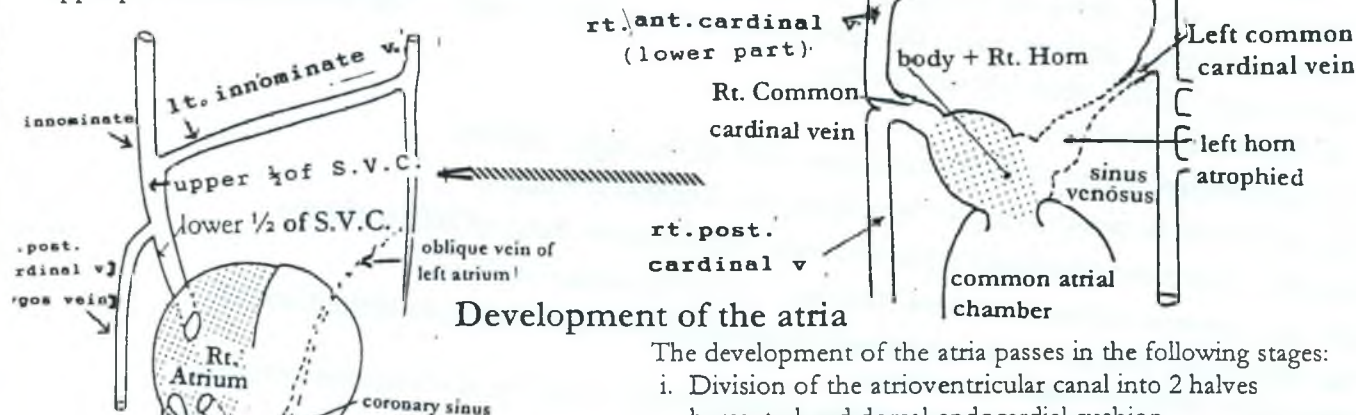


Summary & Illustrations

Fate of the sinus venosus:

- Right horn is absorbed into the right atrium
- Left horn and body are atrophied → coronary sinus
- Left common cardinal vein → oblique vein of left atrium
- Right common cardinal vein → lower 1/2 of S.V.C.

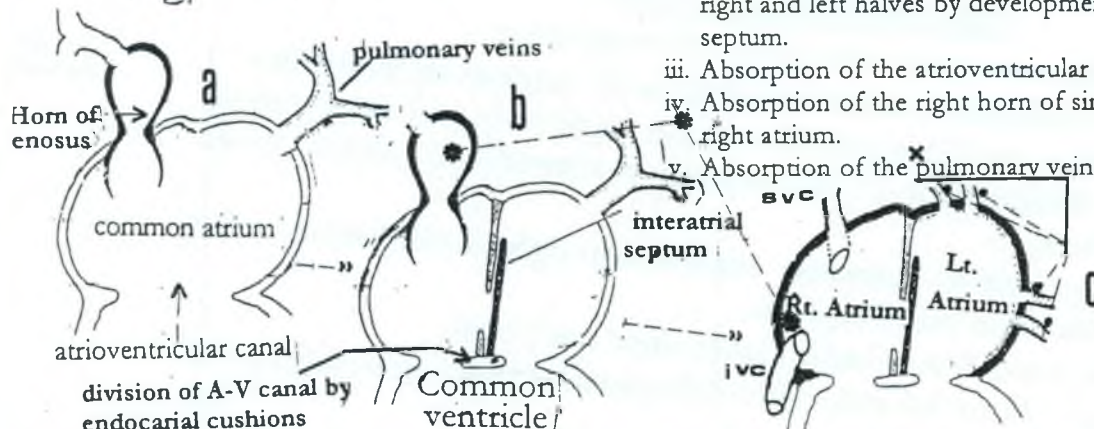
NB. i. The upper 1/2 of SVC develops from the lower part of rt. anterior cardinal vein. ii. The rt. innominate develops from the upper part of the rt. anterior cardinal vein.



Development of the atria

The development of the atria passes in the following stages:

- Division of the atrioventricular canal into 2 halves by ventral and dorsal endocardial cushion
- Division of the primitive common atrium into right and left halves by development of the interatrial septum.
- Absorption of the atrioventricular canal into the 2 atria.
- Absorption of the right horn of sinus venosus into the right atrium.
- Absorption of the pulmonary veins into the left atrium.



Development of the right atrium

The right atrium consists of a smooth part and a rough part.

- The rough part of the atrium (the anterior wall which contains musculi pectinati) is derived from the right 1/2 of the common atrium.
- The smooth part of the atrium (posterior wall) is derived from 2 sources:
 - Right horn of the sinus venosus (mainly).
 - Right 1/2 of the atrio-ventricular canal (slight contribution).
- The right sinus venous valve and septum spurium (which lie between the Rt. horn of the sinus venosus and common atrial chamber) give the crista terminalis, valve of inferior vena cava and valve of coronary sinus.
- The fossa ovalis is formed by septum primum and the annulus ovalis (limbus fossa ovalis) by septum secundum.

Development of the left atrium

The left atrium consists of a rough part and a smooth part.

- The rough part of the atrium is derived from the left 1/2 of the common atrium. It is represented in the adult by the auricle.
- The smooth part of the atrium is derived from 2 sources:
 - i. Absorbed pulmonary veins (common, left & right pulmonary veins).
 - ii. Left 1 / 2 of the atrio-ventricular canal.

-The common, right and left pulmonary veins are absorbed into the wall of the left atrium. As a result the left atrium receives two pulmonary veins from each lung.

NB.

-The common pulmonary vein is formed by the union of right and left pulmonary veins.

-Each of the right and left pulmonary veins is formed by the union of two pulmonary veins from the corresponding lung.

Development of the interatrial septum

This septum is derived from: i. Septum primum & ii. Septum secundum

i. Septum Primum:

-It descends from the roof of common atrium just to the left of sinu-atrial orifice.

-It is sickle-shaped with 2 horns which fuse with the ventral and dorsal endocardial cushions. The foramen bounded by the 2 horns is called ostium primum.

-The ostium primum is gradually closed but before complete closure a new perforation appears in the cephalic part of the septum primum called ostium secundum.

ii. Septum Secundum:

-This septum appears just to the right of the septum primum.

-It is also sickle-shaped with its 2 horns directed caudally towards the atrioventricular cushion.

-The oval gap between the caudal margin of the septum secundum and the cephalic margin of the septum primum is called the foramen ovale.

-The foramen ovale is gradually obliterated, but it may persist in about 30% of subjects.

Embryological remnants of the 2 fetal septa in the adult heart

i. fossa ovalis: represents the part of the septum primum enclosed by the 2 horns of the septum secundum.

i. annulus ovalis or limbus fossa ovalis: represents the free caudal edge of the septum secundum.

Septum Intermedium of the atrioventricular (A-V) canal:

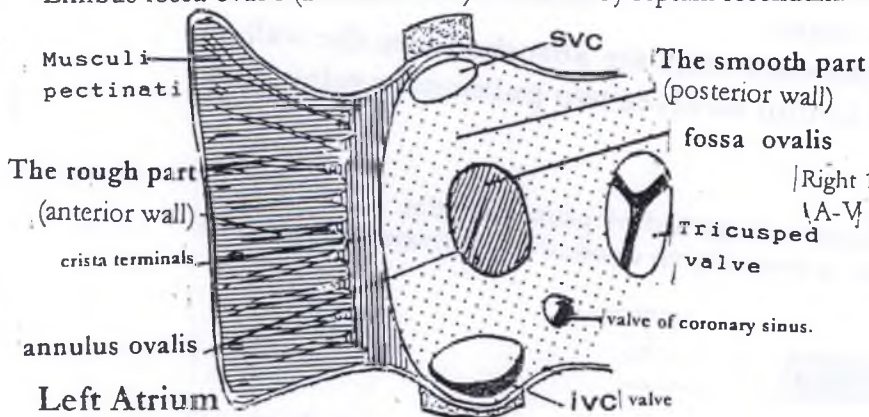
-It is developed in the A-V canal by fusion of the ventral and dorsal endocardial cushions.

-This septum divides the A-V canal into right and left canals.

Summary & Illustrations

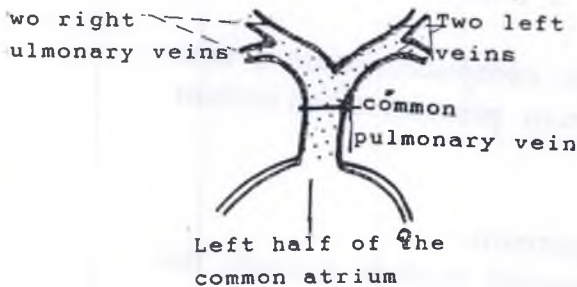
Right Atrium

- The **rough part** (anterior wall) is derived from:
Right half of common atrium
- The **smooth part** (posterior wall) is derived from:
Right horn of sinus venosus + right 1/2 of atrioventricular canal
- Fossa ovalis** is formed by septum primum
- Limbus fossa ovalis** (annulus ovalis) is formed by septum secundum.



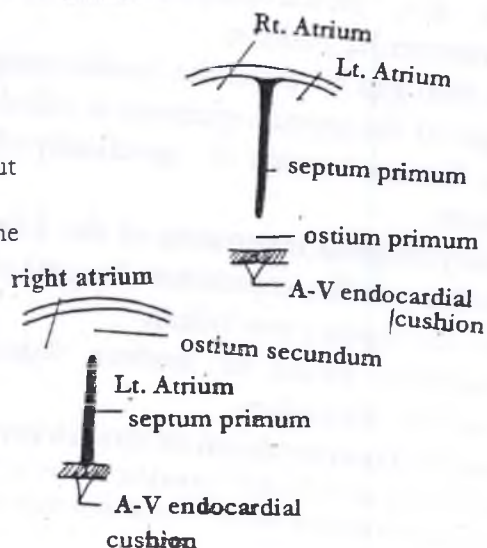
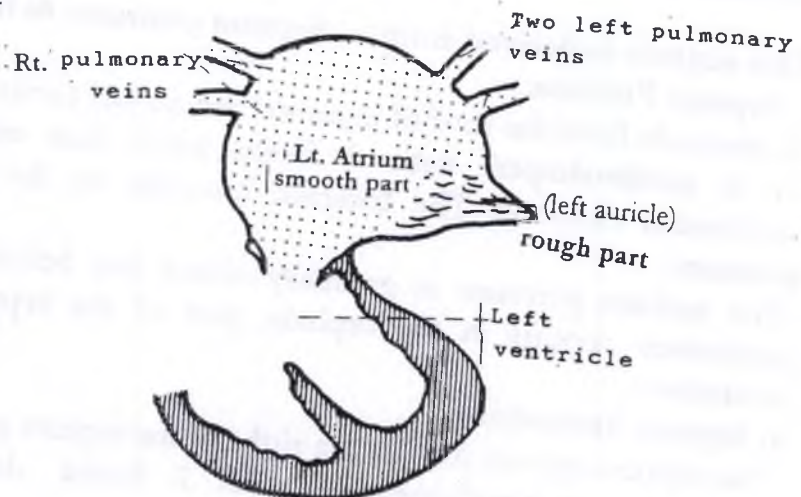
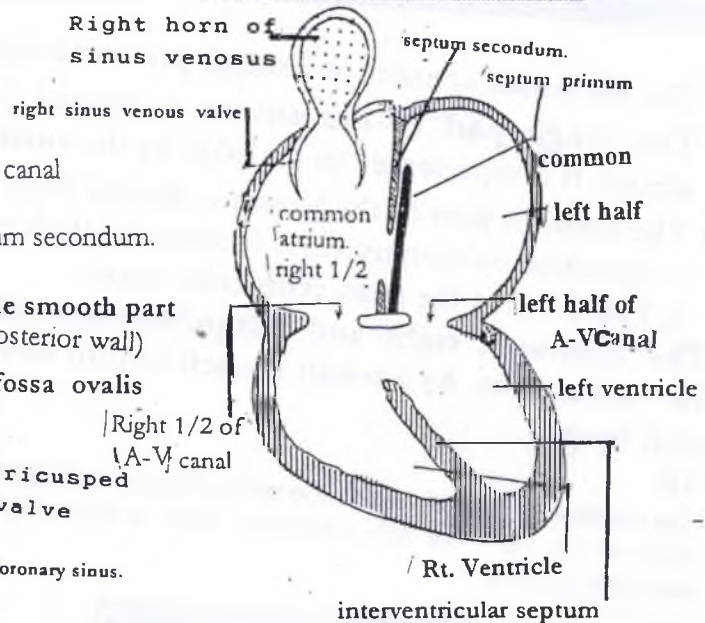
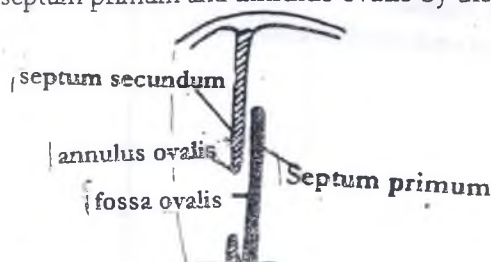
Left Atrium

- The **rough part** (left auricle) is derived from:
left half of common atrium.
- The **smooth part** is derived from:
Absorption of the 4 pulmonary veins +
left 1/2 of the atrioventricular canal.



Interatrial septum

- Septum primum** descends from the roof of the common atrium towards the A-V endocardial cushion.
-It is an incomplete septum leaving a caudal foramen called **ostium primum**
- The septum primum descends to close the ostium primum, but leaving a cephalic foramen called **ostium secundum**.
- A new septum (**septum secundum**) appears to the right of the septum primum.
The **septum secundum** is sickle shaped and descends from the roof of the right atrium to close the ostium secundum gradually.
- After birth, the 2 septa fuse. A **fossa ovalis** is formed by septum primum and **annulus ovalis** by the septum secundum.



Development of the ventricles

The right and left ventricles develop from 2 sources:

i. The common ventricle. ii. The bulbus cordis.

- The bulbus cordis becomes absorbed into the common ventricle to form the **common bulbo-ventricular chamber**. This chamber is then divided into the left and right ventricles by the interventricular septum.
- The **infundibulum** of the right ventricle and **aortic vestibule** of the left ventricle are developed from the bulbus cordis, and form the smooth parts of the right ventricle and left ventricle respectively.

Development of the interventricular Septum

The interventricular (I.V.) septum is developed as follows:

- 1 **The muscular part of the septum:** develops from muscle tissue at the apex of the heart and ascends towards the ventral and dorsal endocardial cushions. It is sickle-shaped and its 2 horns bound the I.V. foramen in the upper part of the septum.
- 2- **The membranous part of the septum:** is formed from: endocardial tissue which fills the I.V. foramen. This tissue is derived from the following sources:
 - A- **extension from the atrioventricular endocardial cushions** which forms the membranous part of the adult septum.
 - B- **Proximal bulbar septum:** separates the infundibulum of right ventricle from the vestibule of the left ventricle.

Distal bullar septum:

Divides the distal part of bulbus cordis into aortic and pulmonary orifices.

Development of the conducting system of the heart:

-The heart beat is initiated from spontaneous contraction of the cardiac myocytes in the **pace maker regions**. This contraction spreads to the rest of the heart through **conduction pathway**.

1. A cluster of **pace maker cells** develop in the sino-atrial region of the sinus venosus to form the **sino-atrial (SA) node** at week 5 of development.
2. A cluster of **pace maker cells** develop in the atrio ventricular region to form the **atrio ventricular (AV) node**.
- 3 A bundle of **conducting cells, the atrio ventricular bundle (bundle of His)**, develops and carries the depolarization into the interventricular septum, right ventricle and left ventricle.

Truncus Arteriosus

-It is the most cranial chamber of the heart tube.

-It is divided into the ascending aorta and pulmonary trunk by the **spiral aortico-pulmonary septum**.

Summary & Illustrations

Development of the ventricles

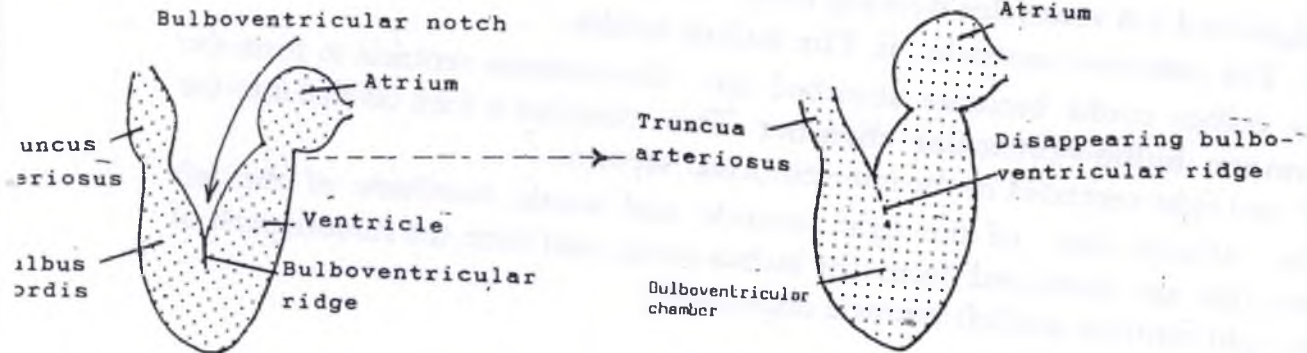
The development of the ventricles passes into 2 stages: i. fusion of the common ventricle and bulbus cordis, ii. division of the bulboventricular chamber into 2 ventricles by the development of the interventricular septum.

i. **Fusion of common ventricle & Bulbus cordis:**

-The **bulbus cordis** becomes **absorbed** into the common ventricle to form **common bulbo-ventricular chamber**. This chamber is divided by the interventricular septum into right and left ventricles.

Summary & Illustrations

Fusion of common ventricle & bulbus cordis (continued)

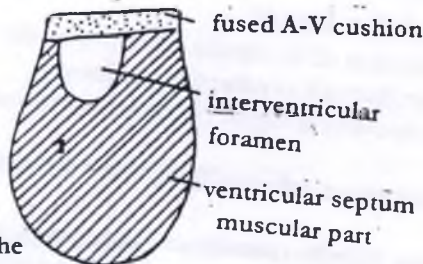
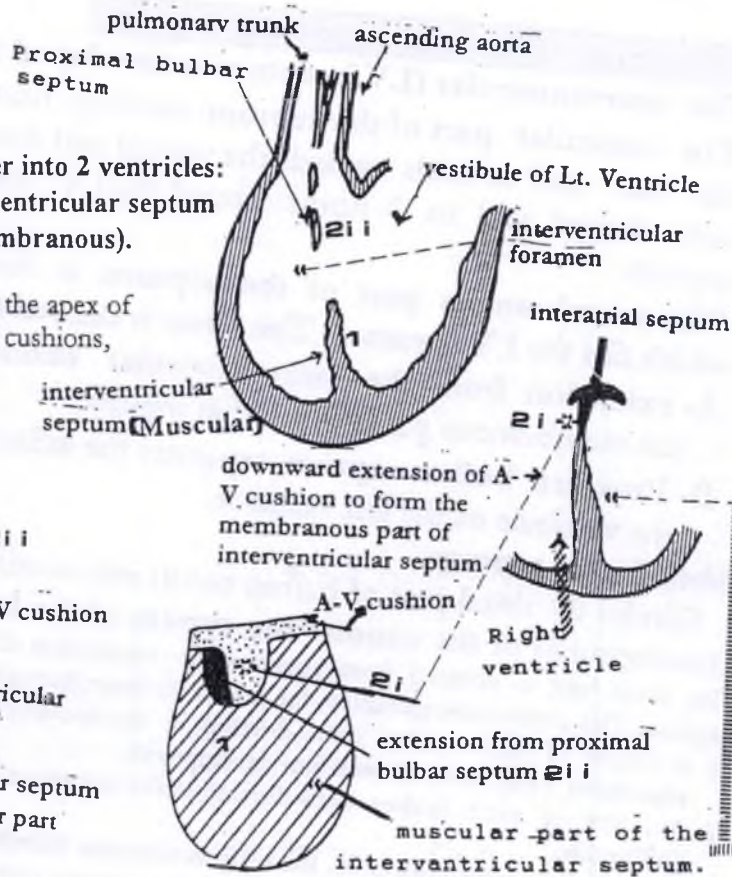


ii. Division of the bulboventricular chamber into 2 ventricles:
This occurs by the development of the interventricular septum which is formed of 2 parts (muscular + membranous).

1. **Muscular part:** sickle shaped, arises from the apex of the heart, ascends upwards to the endocardial cushions, leaving an interventricular foramen.

2. **The membranous part** formed by:

- Extension of A-V cushions. 2 i
- Extension from proximal bulbar septum. 2 i i



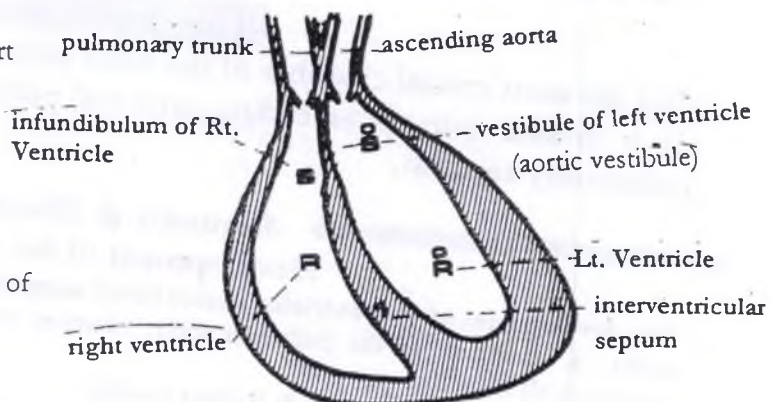
Rt. side view to show the different parts of the interventricular septum

The right ventricle is developed from:

- The rough muscular part from the right part of the common ventricle. **R**
- The smooth part (infundibulum) from the right part of the bulbus cordis. **S**

The left ventricle is developed from:

- The rough muscular part from the left part of the common ventricle. **R**
- The smooth part (aortic vestibule) from the bulbus cordis. **S**



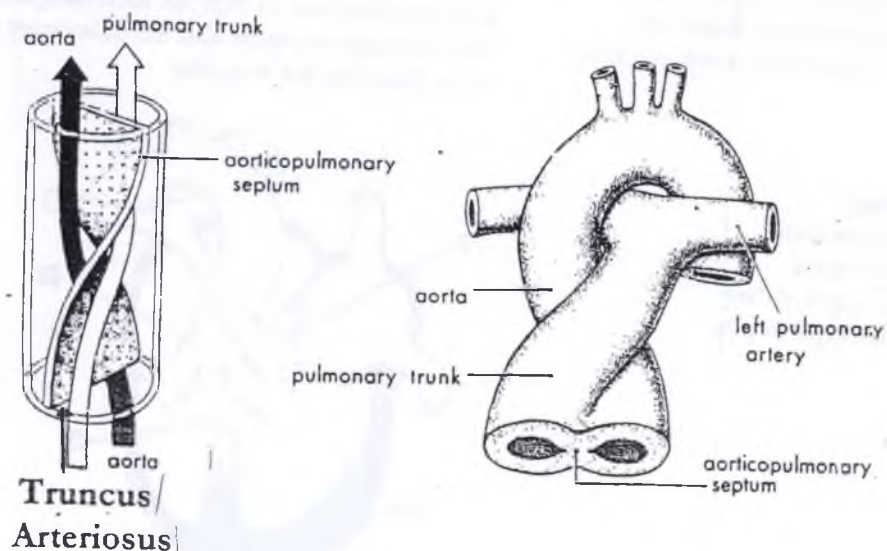
Congenital anomalies heart

1. **Dextrocardia:** The apex of the heart is directed to the right. If it is associated with transposition of abdominal viscera the condition is called **situs inversus**.
2. **Septal defects:**
 - a. **Atrial septal defects:**
 - Patent foramen ovale (the commonest).
 - Patent ostium primum.
 - Complete absence of the interatrial septum.
 - b. **Ventricular septal defects:**
 - Patent I.V. foramen.
 - Presence of a foramen in the muscular part of the I.V. septum.
 - c. **Defects in the aortico-pulmonary septum:**
 - Transposition of the ascending aorta and pulmonary trunk (the septum is twisted in a reverse direction).
 - Aortico-pulmonary window (a foramen in the septum).
 - Complete absence of the septum.
3. **Anomalies of the heart orifices:**
 - Stenosis of the A-V orifice (the right is commonly affected).
 - Abnormally wide A-V orifice.
 - Stenosis of the pulmonary orifice (common).
4. **Multiple anomalies:**
 - a. **Fallot's tetralogy:** in which the patient has 4 combined anomalies.
 - Stenosis of the pulmonary trunk.
 - Overriding of the aorta.
 - Patent I.V. foramen.
 - Hypertrophy of the right ventricle.
 - b. **Eisenmenger's complex:**
 - Overriding of the aorta.
 - Patent interventricular foramen.

Summary & Illustrations

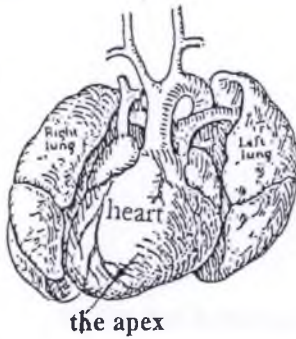
Truncus Arteriosus

Divided into ascending aorta and pulmonary trunk by spiral aortico-pulmonary septum.



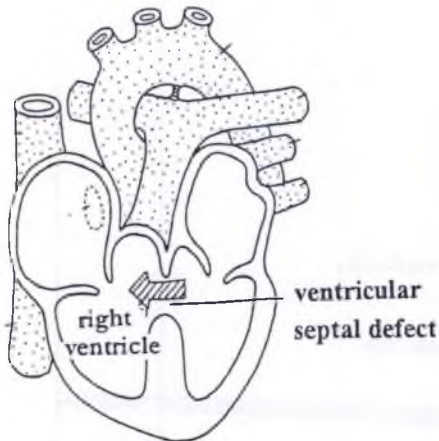
Summary & Illustrations

Commonest anomalies of the heart



1. Dextrocardia

-The apex of the heart is directed to the right



3. Ventricular septal defect

-Most common defect

-It occurs in the membranous part of the interventricular septum due to failure of growth and fusion of the endocardial cushion.

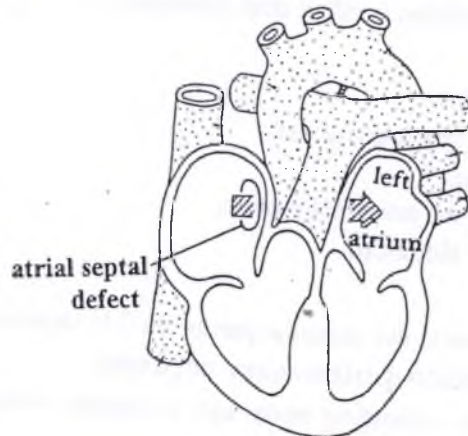
5. Fallot's Tetralogy

1. Pulmonary trunk stenosis

2. Overriding of the aorta

3. Interventricular septal defect

4. Right ventricular hypertrophy.

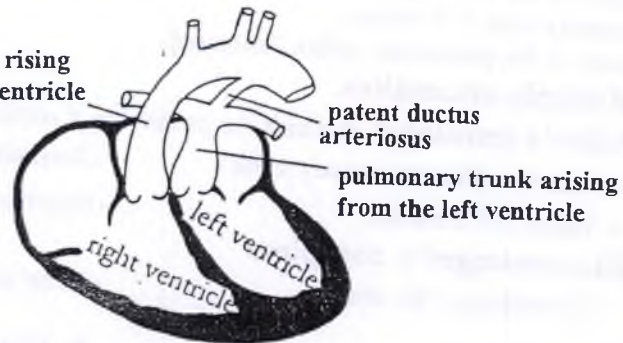


2. Atrial septal defect (patent foramen ovale)

-An opening remains between the right and left atria

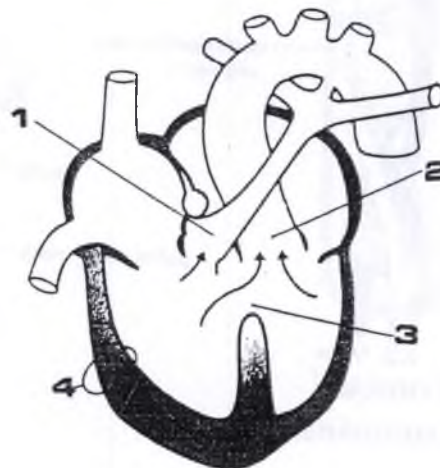
-It is due to underdevelopment of septum secundum or excessive absorption of septum primum.

ascending aorta rising from the right ventricle



4. Transposition of the ascending aorta and pulmonary trunk

The spiral aorto-pulmonary septum is twisted in a reverse direction so that the ascending aorta arises from the right ventricle and the pulmonary trunk arises from the left ventricle



Aortic arches

- The aortic arches are **6 pairs of arteries** situated in the side walls of the pharynx (a set on each side). Each aortic arch lies within a mesodermal thickening called the pharyngeal (**branchial**) arch.
- The aortic arches extend between the **aortic sac** (ventrally) to the 2 **dorsal aortae** (dorsally).
- The fifth aortic arch is rudimentary in man and soon disappears.

Derivatives of the aortic arches:

First: disappears except for a small part which forms the **Maxillary artery**.

Second: disappears except for a small part which forms the **Stapedial artery**.

Third: forms the common carotid artery & the proximal part of the internal carotid artery. External carotid artery arises as a bud from the 3rd arch.

- **Fourth arch forms the arch of aorta on the left side.**
- **Fourth arch forms the subclavian artery on the right side.**
- **Fifth arch disappear** on both sides.
- The ventral part of the **right sixth arch forms the right pulmonary artery**, while its **dorsal part forms the ducts arteriosus**.
- Descending aorta disappears on the right side and the arch on the left side becomes continuous with the descending aorta.
- **Truncus arteriosus** divides into **ascending aorta** and **pulmonary trunk**.

NB. It is said by some authors that the proximal part of the arch of aorta and distal parts of the ascending aorta and pulmonary trunk are derived from a dilatation, called **aortic sac**, at the upper end of the truncus arteriosus.

- **The ascending aorta becomes continuous with the arch** (fourth arch).
- **The pulmonary trunk becomes continuous with the pulmonary arteries** (sixth arches).

• Fate of aortic sac:

- 1- **The right horn:** form the brachiocephalic (innominate) artery which is continuous with the right common carotid (of the right 3rd aortic arch) & with the stem of the right subclavian artery (of the 4th right aortic arch).
- 2- **The stem + the left horn:** form the proximal part of the arch of the aorta.

• Fate of the right & left dorsal aortae:

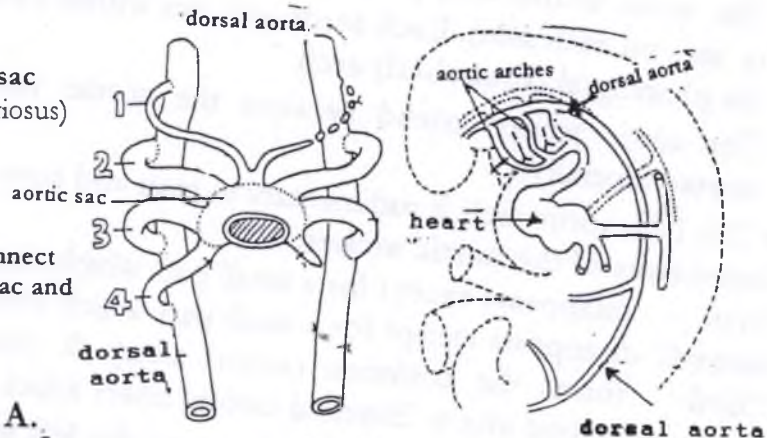
- 1- **The segment cranial to the 3rd aortic arch.** Forms the distal part of the internal carotid a. on both sides.
- 2- **The segment between the 3rd & 4th aortic arches:** disappears in both sides.
- 3- **The segment of the right dorsal aorta between the 4th arch & 6th arch:** forms part of the right subclavian artery.
- 4- **The segment of the left dorsal aorta between the 4th arch & 6th left arch:** forms the distal part of arch of aorta.
- 5- **The segment of the right dorsal aorta caudal to the 6th arch degenerates.**
- 6- **The segment of the left dorsal aorta caudal to the 6th arch persists to form the descending aorta.**

Summary & Illustrations

Aortic arches

- 6 pairs of arteries (aortic arches), each one belongs to one of the 6 pharyngeal arches.
- Each aortic arch extends between the **aortic sac** (dilatation at the upper end of the ductus arteriosus) to the **dorsal aorta**.

the aortic arches connect between the aortic sac and dorsal aorta



Fate of the aortic arches

- 1st arch disappears (leaving maxillary artery)
- 2nd arch disappears (leaving stapedial artery)
- 3rd arch gives carotid arteries:

- External carotid arises as a new branch from the 3rd arch.
- Proximal to the external carotid the 3rd arch gives the common carotid artery
- Distal to the external carotid the 3rd arch gives the internal carotid artery

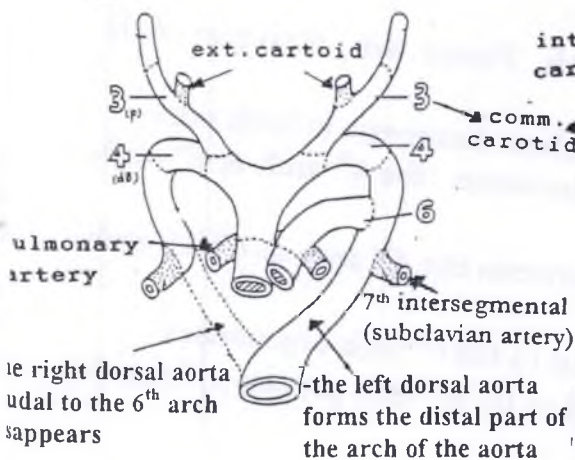
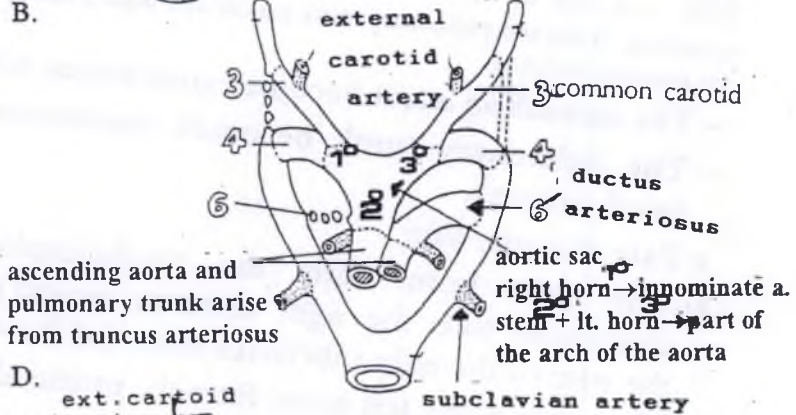
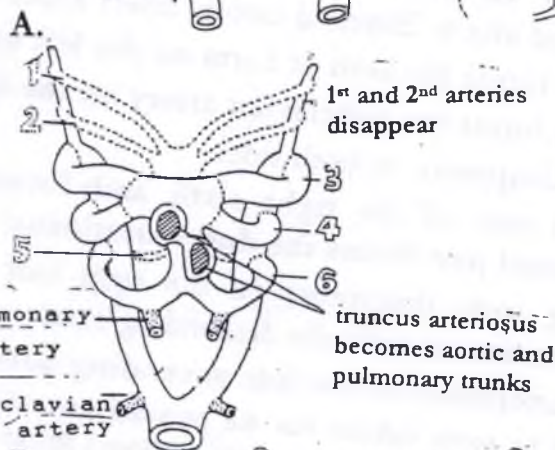
4th arch on the right side: it gives the proximolateral part of subclavian artery. On the left side it gives part of the arch of the aorta.

- 5th arch disappears

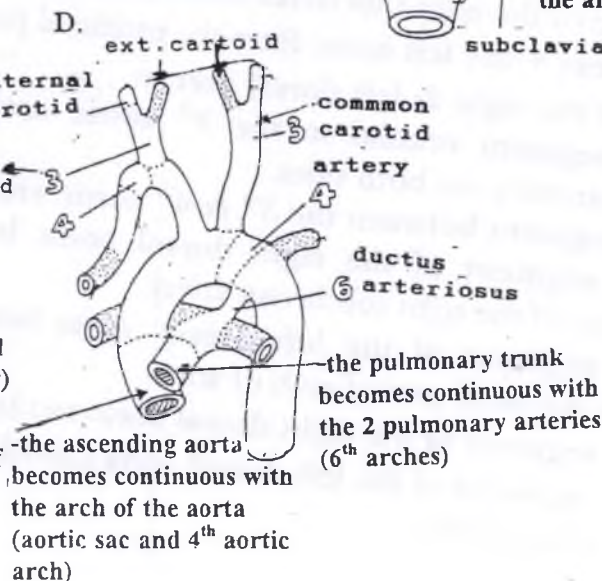
- 6th arch: The proximal part of each side gives the corresponding (right or left) pulmonary artery.

- The distal part of the right side disappears

- The distal part of the left side forms the ductus arteriosus.



ascending aorta and pulmonary trunk arise from truncus arteriosus



Summary & Illustrations

Arch of the aorta

The arch of the aorta in the adult develops from the following sources:

- A Proximal part (proximal to the origin of the innominate artery): arises from the **stem of the aortic sac**.
- B. Its middle part (between the innominate and left common carotid artery): arises from the **left horn of aortic sac**.
- C. Its distal part (distal to common carotid artery): arises from 2 sources:
 - i. The left 4th aortic arch
 - ii. The lower part of the left dorsal aorta down to the 7th intersegmental artery (subclavian artery).

Relation of recurrent laryngeal nerves to the aortic arches:

Each vagus nerve gives a recurrent laryngeal nerve which hooks around the dorsal part of the 6th arch to reach the developing larynx.

As development proceeds the following occurs:

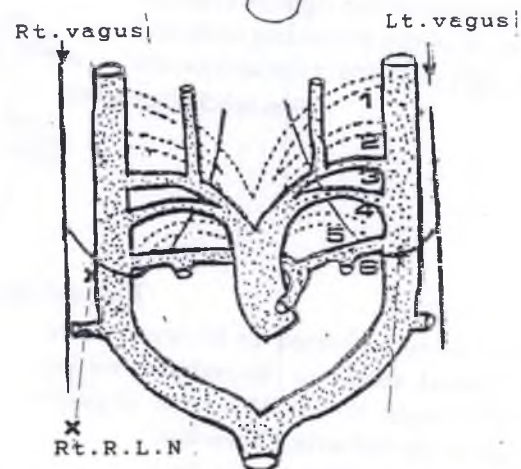
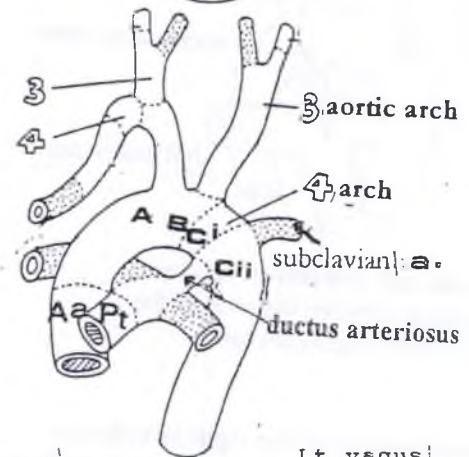
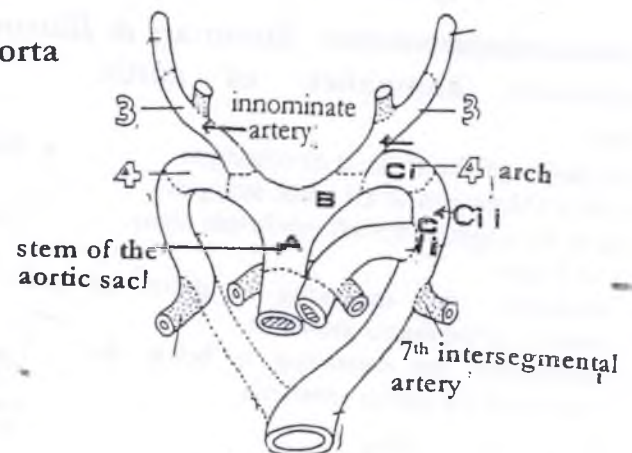
a. On the right side:

The dorsal part of the 6th arch + 5th arch **degenerate** leaving the right recurrent laryngeal nerve hooking around the 4th right aortic arch which forms the **right subclavian artery**. Therefore, the right recurrent laryngeal nerve hooks around the right subclavian artery.

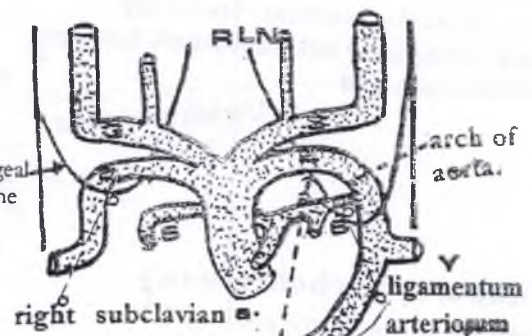
b. On the left side:

The left recurrent laryngeal nerve remains hooking around the dorsal part of the **left 6th arch** which **does not disappear**, but forms the **ductus arteriosus**.

After obliteration of the ductus arteriosus and formation of the ligamentum arteriosum which is overlapped by the arch of the aorta the **left recurrent laryngeal nerve** becomes hooking around the arch of the aorta.



right recurrent laryngeal nerve hooks around the right subclavian artery.



left recurrent laryngeal nerve hooking around the arch of the aorta

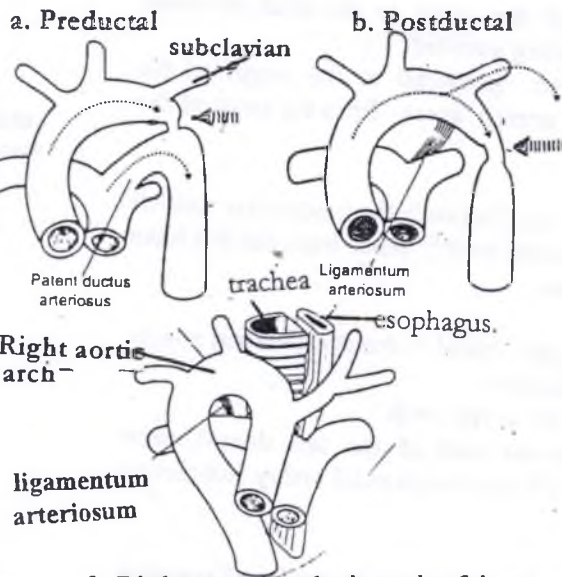
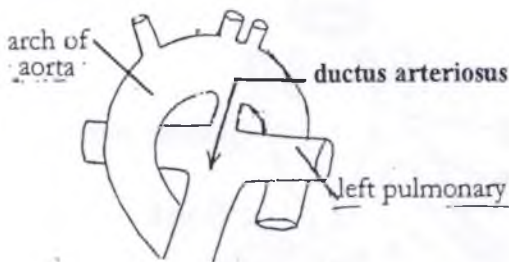
Summary & Illustrations

Commonest anomalies of aortic arches:

Coarctation of the aorta: is narrowing or complete obliteration of the aortic arch just distal to the origin of the left subclavian artery.

It is of 2 types:

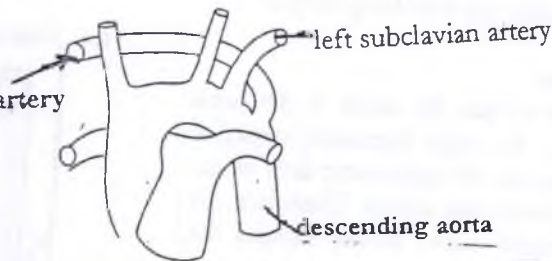
- Preductal:** the narrowing is above the entrance of the ductus arteriosus.
- Postductal:** the narrowing is below the entrance of the ductus arteriosus.



2. Patent ductus arteriosus: results in communication between the arch of the aorta and the left pulmonary artery.

3. Right aortic arch: the arch of the aorta is directed towards the right. It is called by obliteration of the left 4th aortic arch and the left dorsal aorta, while the similar vessels on the right persist.

4. Abnormal origin of the right subclavian artery: it arises from the descending aorta and course to the right side behind the trachea and esophagus.

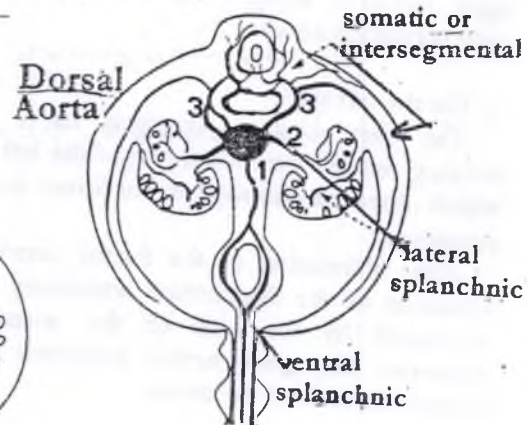
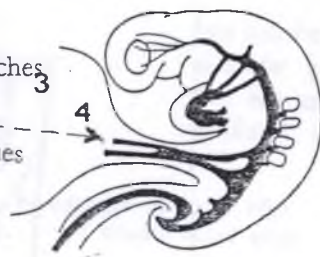


Dorsal Aorta

The dorsal aorta is formed by the union of the Rt. & Lt. Dorsal aortae in the region extending from the 4th thoracic to the 4th lumbar segment (somite). It gives the following branches:

- Ventral (ventral splanchnic) branches. 1
- Lateral (lateral splanchnic) branches. 2
- Dorsal (somatic or intersegmental) branches. 3
- Umbilical arteries. 4

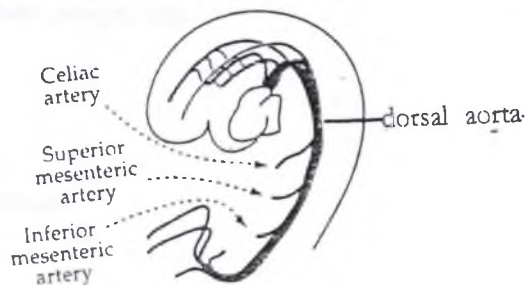
Umbilical arteries



1. Ventral splanchnic arteries

— form the arteries of the gut:

- coeliac artery.
- superior mesenteric artery.
- inferior mesenteric artery.



Summary & Illustrations

Dorsal aorta (continued)

2. Lateral Splanchnic Arteries

Supply the derivatives of the intermediate mesoderm (intermediate cell mass):

1. middle suprarenal arteries.1
2. renal arteries.2
3. testicular or ovarian arteries.3

3. Dorsal (somatic or intersegmental) arteries

These are paired branches (Rt. & Lt.) which arise from the posterolateral aspect of the dorsal aorta & pass laterally between the somites.

- supply the body wall.
- divide into dorsal and ventral branches.
- represented by:
 - i. intercostal arteries.
 - ii. subcostal arteries.
 - iii. lumbar arteries.
- They are connected together by **longitudinal anastomoses**:

1. **Ventral anastomosis**: which forms the internal mammary, superior epigastric and inferior epigastric arteries.

2. **Dorsal anastomoses**:

A. **Precostal anastomosis**: which gives the ascending cervical and superior intercostal arteries.

B. **Postcostal anastomosis**: which gives the second part of the vertebral artery.

C. **Post-transverse anastomosis**: which gives the deep cervical artery.

4. Umbilical arteries (Rt. & Lt.)

A- At first, they arise from the dorsal aorta.

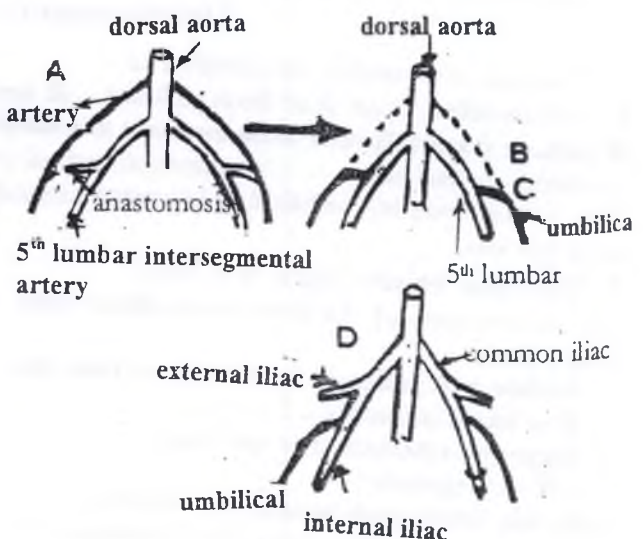
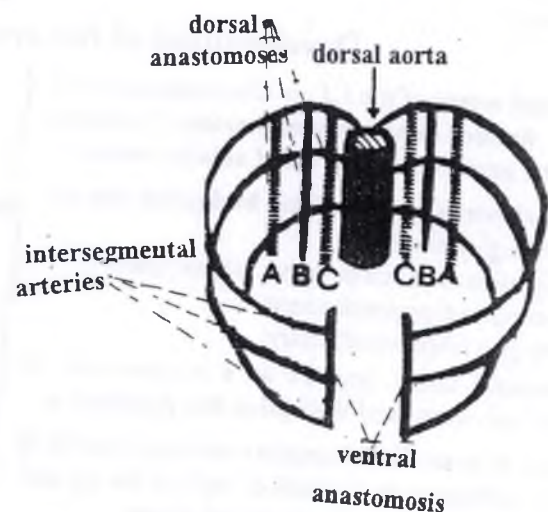
B- Then they become connected to the 5th lumbar intersegmental artery by an anastomosis.

C- Then they lose their connection to the dorsal aorta.

D- The external iliac artery arises as a branch of the 5th lumbar intersegmental artery leaving the umbilical artery attached to its distal part which becomes the internal iliac artery. The proximal part of the 5th lumbar intersegmental artery now becomes the common iliac artery.

E- The proximal parts of the umbilical arteries give the superior vesical arteries to urinary bladder.

F- After birth, the distal parts of the umbilical arteries obliterate forming **lateral umbilical ligaments**.



Summary & Illustrations

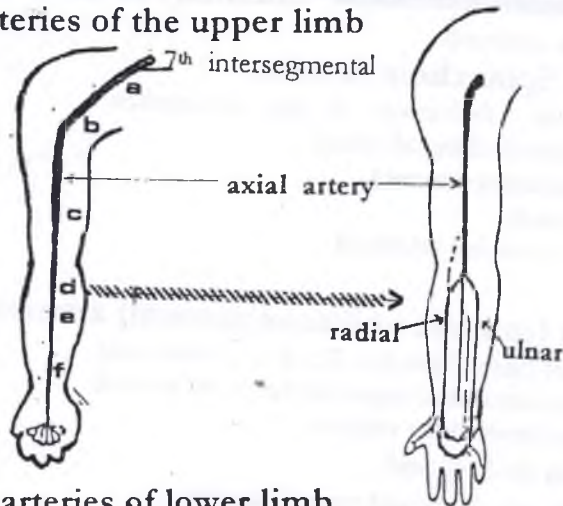
Development of the arteries of the upper limb

The arteries of the upper limb develop from an axial artery which runs in the axis of the limb.

- The **axial artery** of the upper limb bud arises from the 7th intersegmental artery & proceeds distally gives rise to:

- part of subclavian artery.
- axillary artery.
- branchial artery.
- part of ulnar artery.
- common interosseous artery.
- anterior interosseous artery.

- The **ulnar** and **radial** arteries appear as branches of the axial artery.



Development of the arteries of lower limb

• The **axial artery** of the L.L. is the continuation of the 5th lumbar intersegmental artery. It follows the sciatic nerve, hence it is called **sciatic artery**.

• The **axial artery** of lower limb bud gives rise to

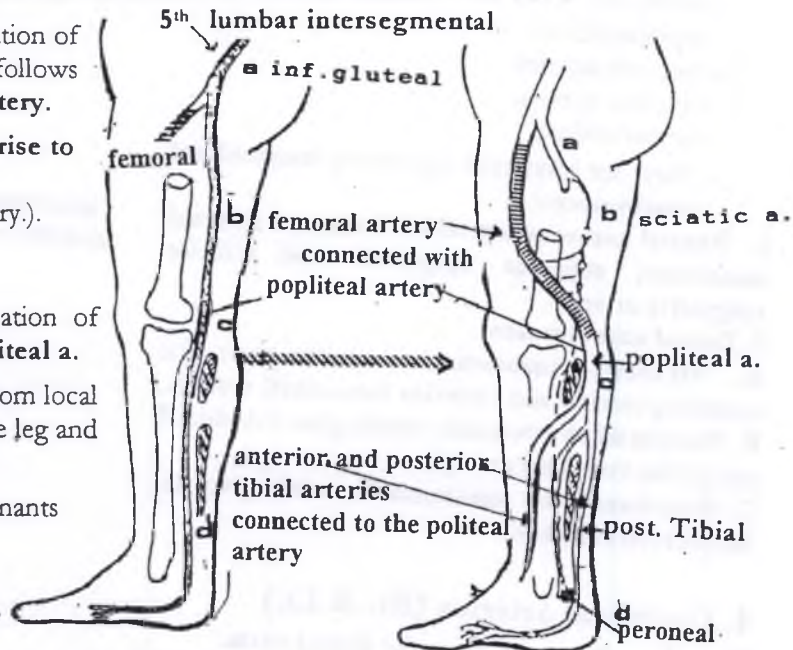
- inferior gluteal artery.
- companion a. of sciatic nerve (sciatic artery.).
- upper part of popliteal artery.
- lower part of peroneal artery.

- the **femoral artery** appears as a continuation of external iliac artery, and then joins the **popliteal a.**

• the **ant. & post. Tibial arteries** develop from local vascular plexuses in the front & back of the leg and become **connected to the popliteal artery**.

• the **axial artery then degenerates**, its remnants in the adult L.L. are represented by:

1. inf. Gluteal artery.
- 2- sciatic artery.
3. longitudinal anastomosis in the back of thigh.
4. peroneal artery in the back of leg.



Development of the veins

The veins of the embryo are identified as:

1. vitelline veins. Drain blood from yolk sac. **2 umbilical veins.** Carry oxygenated blood from placenta

3 somatic (cardinal) veins drain the body of embryo itself on each side:

- a. anterior cardinal vein.
- b. common cardinal vein (duct of Cuvier).
- c. posterior cardinal vein.

The 3 veins (vitelline, umbilical and common cardinal) from each side open into the corresponding horn of the sinus venosus.

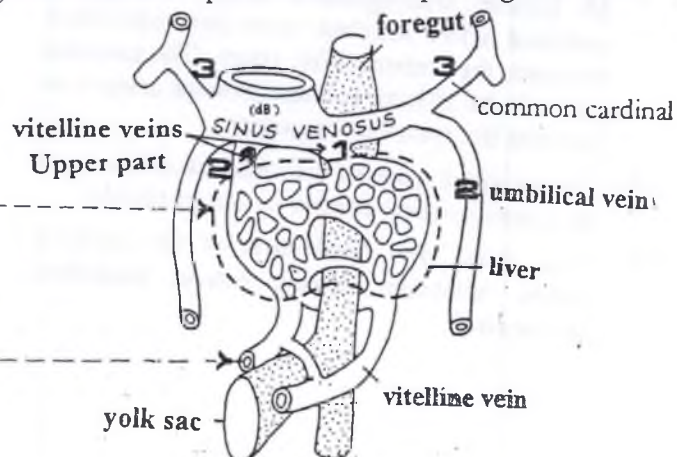
1. Vitelline veins: (right and left)

The development of the liver divides these veins into 3 parts:

- Middle part** (inside the liver) breaks to form the liver blood sinusoids.
- Upper part** (between liver and heart)
left vein regresses

right vein forms suprahepatic part of IVC.

- Lower part** (caudal to liver) The 2 vitelline veins join each other by three anastomoses to form the portal venous system.



Summary & Illustrations

Development of the veins (continued)

2. Umbilical veins: (right and left)

The part of these veins inside the liver breaks and shares in the formation of liver sinusoids.

Below the liver:

- The right umbilical vein disappears.
- The left umbilical vein persists throughout intrauterine life and carries oxygenated blood from placenta to the left branch of portal vein.
- A channel is formed between the left branch of portal vein and upper part of I.V.C. This is called **ductus venosus** and carries oxygenated blood.
- After birth, the left umbilical vein becomes fibrosed and transformed into **ligamentum teres**.

3. Cardinal veins

a) Anterior Cardinal vein:

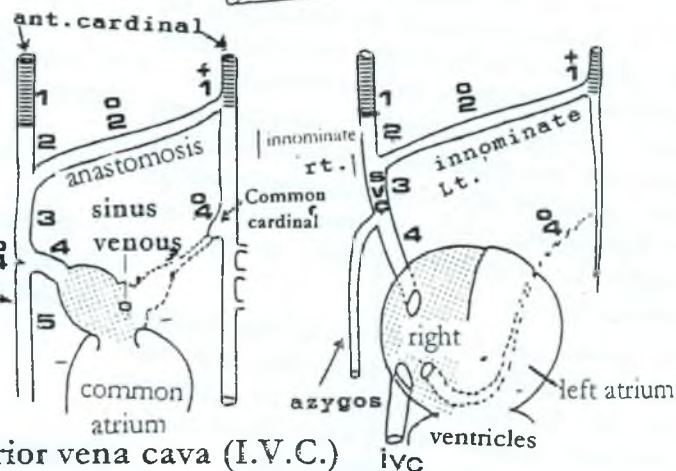
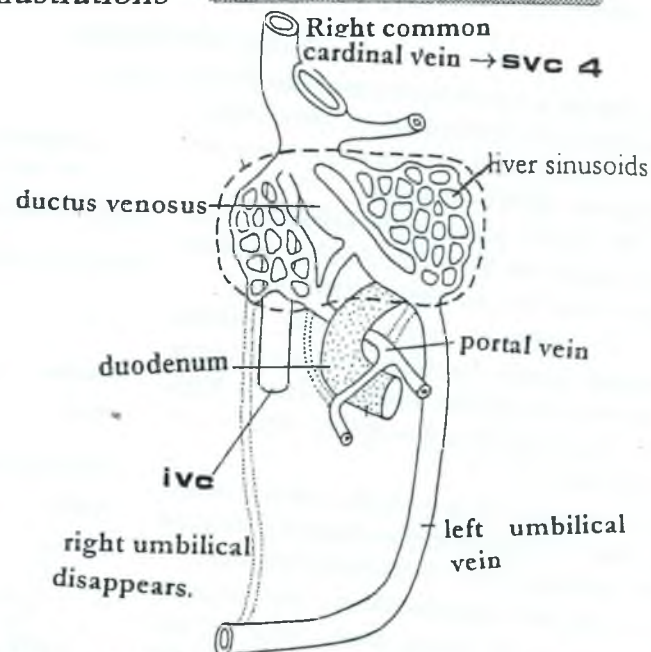
- On the right side: forms the right internal jugular¹ vein, right innominate² vein and upper part of SVC.³
- On the left side: forms left internal jugular vein.¹
- The left innominate² vein develops as a transverse anastomosis between the 2 anterior cardinal veins.

b) Common cardinal vein (Duct of Cuvier):

- On the right side: forms the lower part of s.v.c.⁴
- On the left side: forms oblique vein of left atrium.⁴

c) Posterior cardinal vein:⁵

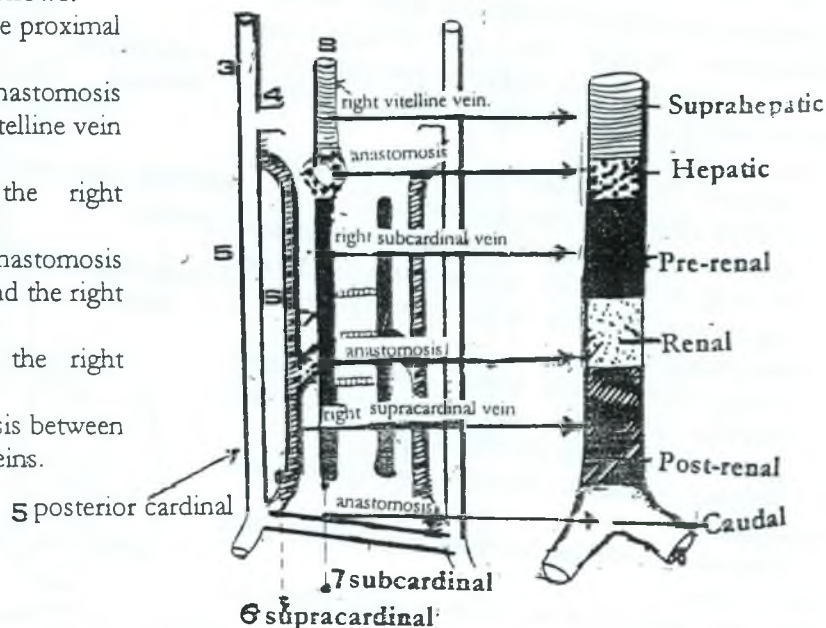
- gradually disappear & replaced by the **supracardinal⁶** and **subcardinal⁷** veins.
- several anastomoses connect these veins.



Development of the inferior vena cava (I.V.C.)

It develops from several segments as follows:

- 1 **Suprahepatic part** develops from the proximal part of right vitelline veins⁸
- 2 **Hepatic part** develops from the anastomosis between the proximal part of right vitelline vein and the right subcardinal vein.
3. **Pre-renal part** develops from the right subcardinal vein.⁷
4. **Renal part** develops from the anastomosis between the right subcardinal vein and the right supracardinal vein.
5. **Post-renal part** develops from the right supracardinal veins⁶
6. **Caudal part** develops from anastomosis between caudal ends of the posterior cardinal veins.



Fetal circulation

Oxygenated blood is carried by the **umbilical vein (left)** from the placenta to the **left branch of portal vein**.

Most of this blood passes to the inferior vena cava directly through the **ductus venosus**.

Some of the blood passes to the branches of the portal vein to reach the liver. This blood is collected by the hepatic veins into the inferior vena cava.

- Blood of **inferior vena cava** (better oxygenated) passes into the right atrium where it is directed through the foramen ovale to reach the left atrium and then through the mitral valve to the left ventricle.
- Blood of **superior vena cava** (non-oxygenated) passes into the **right atrium** where it is directed through tricusped valve to the **right ventricle**.
- Blood of the **left ventricle** (better oxygenated) passes into the **ascending aorta**. Most of this blood is distributed through the **branches of the arch of aorta** to the head, neck and upper limbs. A small amount passes to the descending aorta.
- Blood of **right ventricle** (non-oxygenated) passes into the **pulmonary trunk**. Most of this blood passes through the **ductus arteriosus** into the **descending aorta**. A small amount passes through the pulmonary arteries to the non functioning lungs.
- The greater part of the blood of **descending aorta** passes into the common iliac artery and then into the internal iliac artery to reach the **umbilical arteries** which carry blood to the placenta where oxygenation occurs.

Changes in fetal circulation after birth:

• **Immediate changes:** The cord is ligated and cut the **foramen ovale** is closed by pressure of the septum primum against the septum secundum. This is due to 2 main factors:

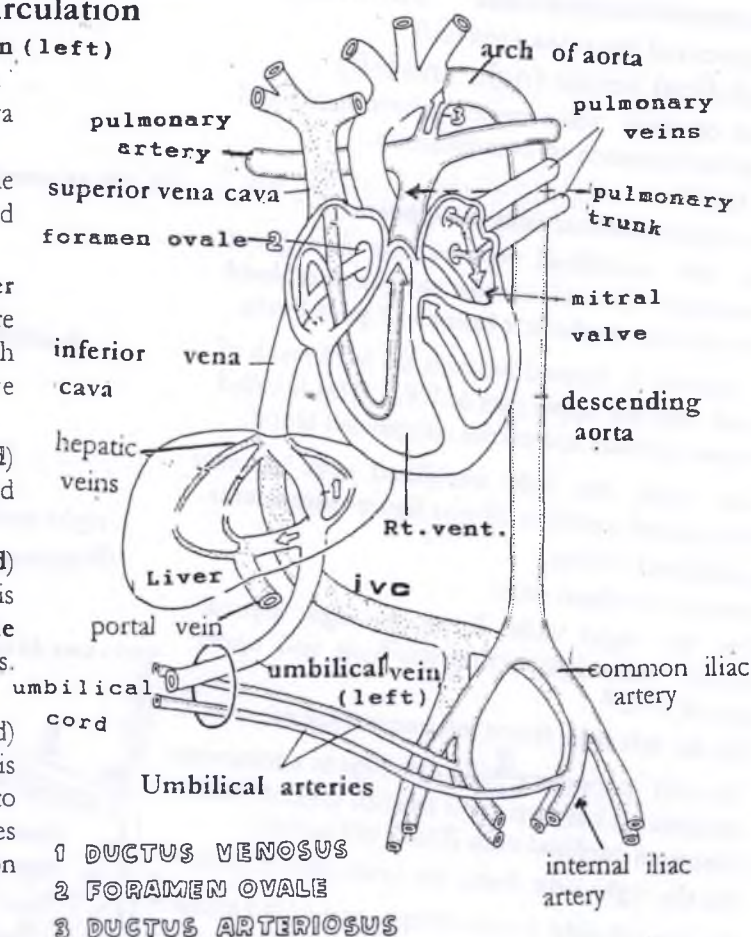
- Occlusion of left umbilical vein and diminution of blood returning to the right ventricle.
- Inflation of the lungs by the start of respiration (at birth) and increase of the amount of blood returning to left atrium via the pulmonary veins.

• Late changes:

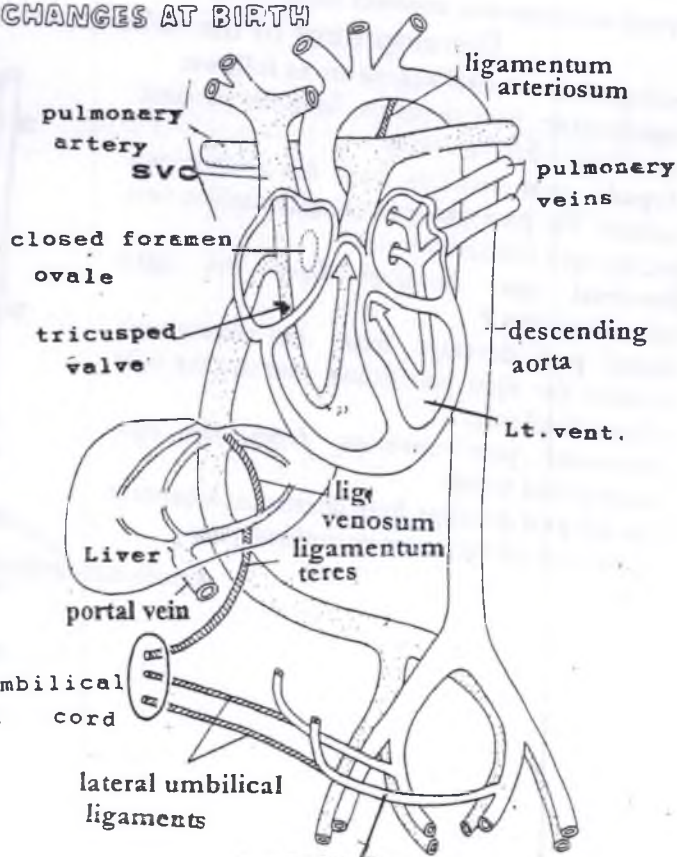
During the first few months after birth some **vascular channels are transformed into ligaments**; these are the following:

- 1- **Ductus venosus**: becomes the **ligamentum venosum**.
- 2- **Ductus arteriosus**: becomes the **ligamentum arteriosum**.
- 3- **(Left) umbilical vein**: becomes the **ligamentum teres of the liver**.

Umbilical arteries: become the **lateral umbilical ligaments**.



CHANGES AT BIRTH



DEVELOPMENT OF THE NERVOUS SYSTEM

- The nervous system develops from the **neural plate** which differentiates from the **ectodermal layer of the embryonic disc**.
- The margins of the neural plate are raised to form the **neural folds**.
- The neural plate is then converted into **neural groove**.
- The neural folds fuse and the neural groove is transformed into the **neural tube** by the 4th week of intra-uterine life.
- The tube has 2 temporary openings called the **anterior, posterior neuropores** which are ultimately closed.
- The **cranial part** of the tube dilates to **form the brain vesicle**, while its **caudal part forms the spinal cord**.

NB. The neural crest is developed at the fusion of the neural folds from the margins of the neural groove.

It appears as 2 cell cords on both sides of the neural tube.

Development and histogenesis of the spinal cord

- The spinal cord develops from the caudal part of the neural tube,
- The tube is originally composed of one layer of simple columnar epithelium surrounding an oval central canal.
- Later on, this layer proliferates & the **neural tube** becomes formed of 2 thick **lateral walls** connected by a thin **roof plate** & a thin **floor plate**.
- The **lateral walls** differentiate into 3 layers: (inner **ependymal**, middle **mantle** & outer **marginal**)
 - i. **Inner ependymal layer**: the cells of which give rise to:
 - a. the **ependymal cells** lining the central canal of the spinal cord.
 - b. the primitive nerve cells (**neuroblasts**) which migrate to the mantle layer to form the neurons (nerve cells) of the grey mater.
 - c. **glioblasts (spongioblasts)** which migrate to the mantle layer to form the neuroglial cells.
 - ii. **Middle mantle layer**: formed of nerve cells (**neuroblasts**) & neuroglial cells (**glioblasts**) which form the **grey mater**.
 - iii. **Outer marginal layer**: formed of nerve fibres (ascending & descending tracts) which constitute the **White mater**.
- A groove called **sulcus limitans** appears on the inner surface of the lateral wall on either side dividing it into.
 - An **alar lamina (plate)** posteriorly which contains **sensory cells** and forms the **posterior horn** of the spinal cord.
 - A **basal lamina (plate)** anteriorly, contains **motor cells** & forms the **anterior horn** of the spinal cord.

Enlargements are formed in the cervical & lumbar regions of the spinal cord & the central canal becomes narrow.

Summary & Illustrations

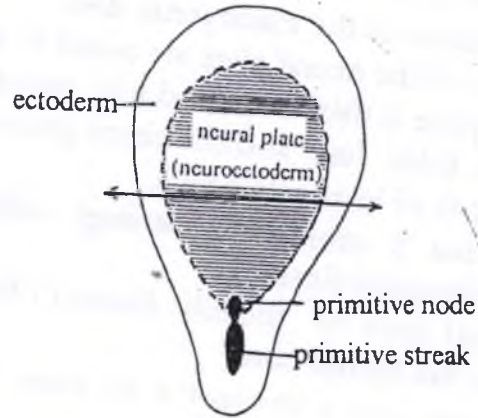
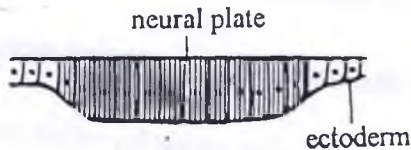
Development of the nervous system

The nervous system develops from the **neural plate**.

Neural plate:

is thickening of the central part of the ectoderm.

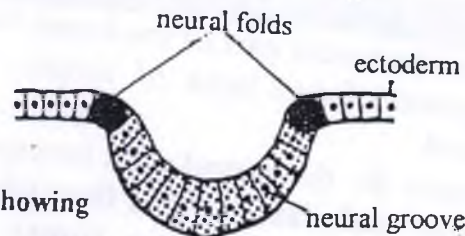
TS in the ectoderm



Neural folds and groove

The margins of the neural plate are raised to form **neural folds**.

The neural plate → **neural groove**.

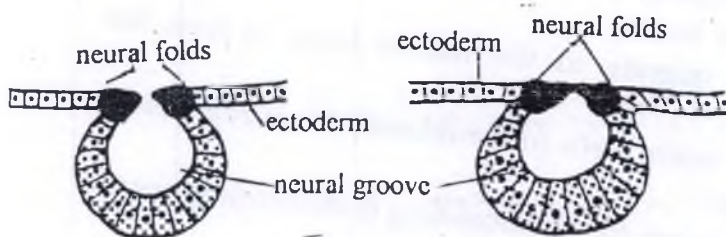


TS in the ectoderm showing the neural groove

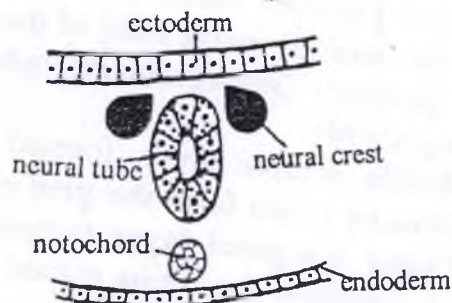
Neural tube

The neural folds fuse and the neural groove → **neural tube**

Neural crest is separated



Transverse sections showing the formation of the neural tube

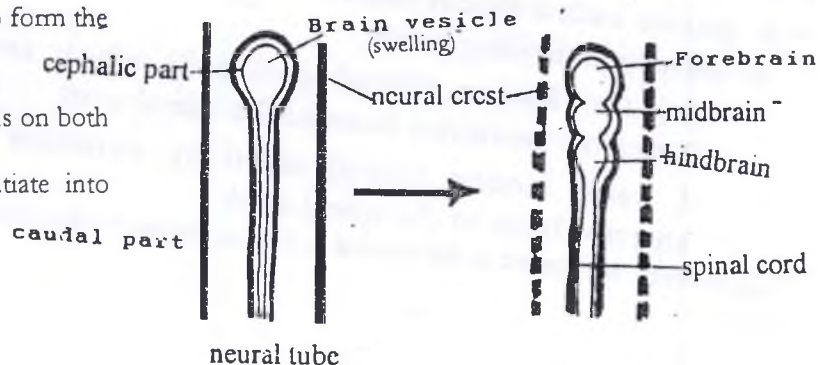


The **cranial part** of the tube dilates to form the **brain vesicle** (swelling)

The **caudal part** forms the **spinal cord**

The **neural crest** appears as 2 cell cords on both sides of the neural tube.

The crest cells migrate and differentiate into many derivatives.



Growth of the spinal cord:

- Till the 3rd month of the intrauterine life the spinal cord fills the vertebral canal completely.
- The vertebral column grows more rapidly than the spinal cord and as a result the caudal part of the cord is stretched to form the **filum terminale**.
- Its lower end reaches the level of the 3rd lumbar vertebra at the time of birth.
- By the 3rd month after birth it ascends to its adult position opposite the disc between the 1st and 2nd lumbar vertebrae.

* **Myelination** of the nerve fibres in the spinal cord begins in the 4th month of intra-uterine life & it is completed by the end of the 1st year of post natal life.

Development of the spinal meninges:

- i. The **dura mater**: develops from **mesoderm** of sclerotomes which form the vertebral column.
- ii. The **arachnoid & pia mater** (leptomeninges): develop from neural crest (**ectodermal** in origin).

Anomalies of the Spinal cord

- 1- **Spina bifida occulta**: due to failure of fusion of the dorsal parts of one of the vertebrae around the spinal cord. This condition occurs commonly in the lumbosacral region & the affected site is covered by hairy skin.
- 2- **Meningocele**: due to failure of fusion of the dorsal parts of 2 or 3 vertebrae. The meninges bulge through the defect.
- 3- **Meningo-myelocele**: like the previous condition but here spinal cord bulges through the defect.
- 4- **Myelocele**: due to failure of closure of the neural tube & the affected part of the spinal cord remains exposed to the surface through the defect in the vertebral canal.

Summary & Illustrations

Development of the spinal cord

-It is developed from the caudal part of the neural tube. A.

-Originally, it is composed of a layer of columnar epithelium, which proliferates.

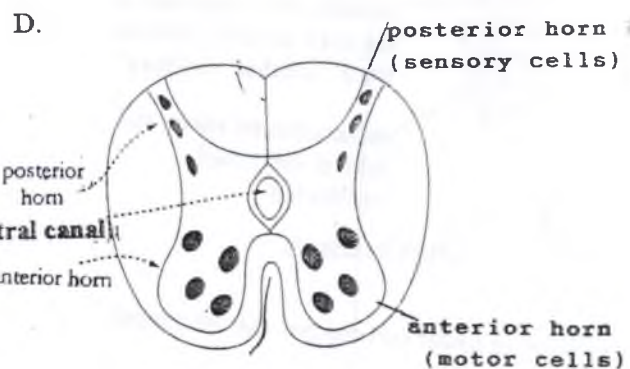
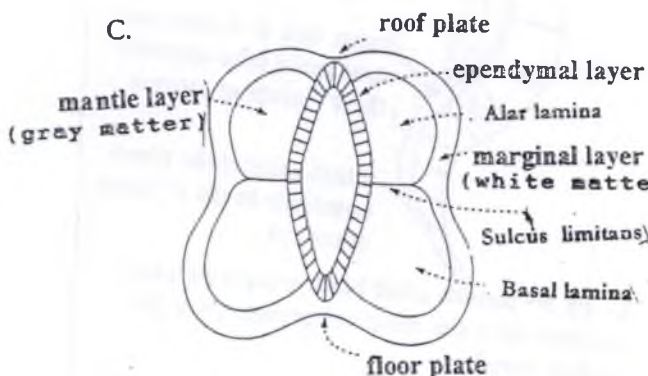
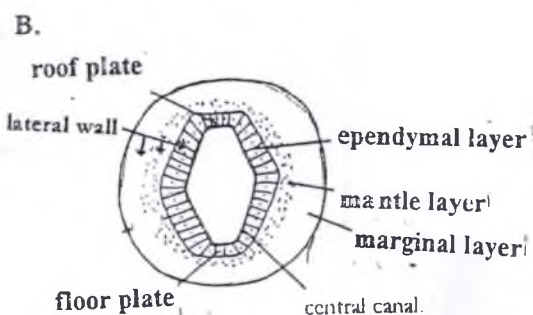
-Later on, the tube has 2 thick lateral walls + thin roof and floor plates.

• The lateral wall differentiates into 3 layers:

- i. Inner ependymal → lining the central canal.
- ii. Middle mantle → the gray matter
- iii. Outer marginal constitute the white matter.

• **Sulcus limitans** appears dividing the lateral wall into:

- a. **Alar lamina** (sensory cells) → posterior horn
- b. **Basal lamina** (motor cells) → anterior horn.



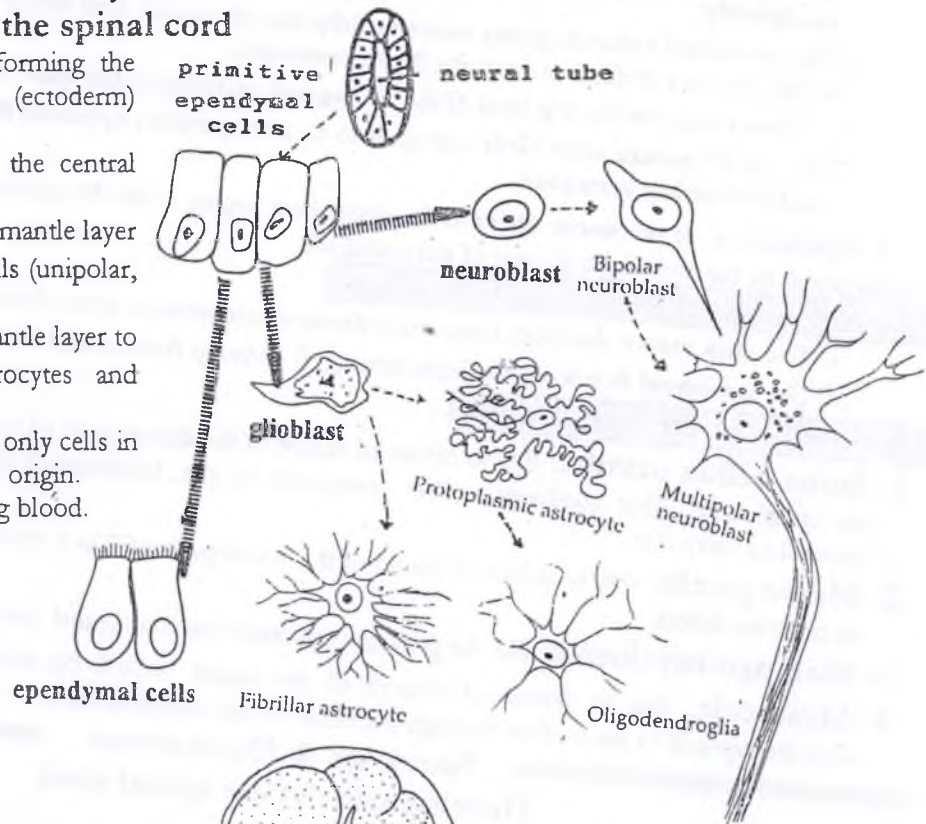
Summary & Illustrations

Histogenesis of the cells of the spinal cord

The primitive ependymal cells forming the wall of the neural tube (ectoderm) differentiate into:

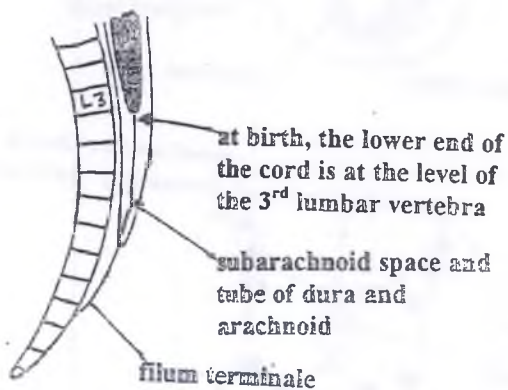
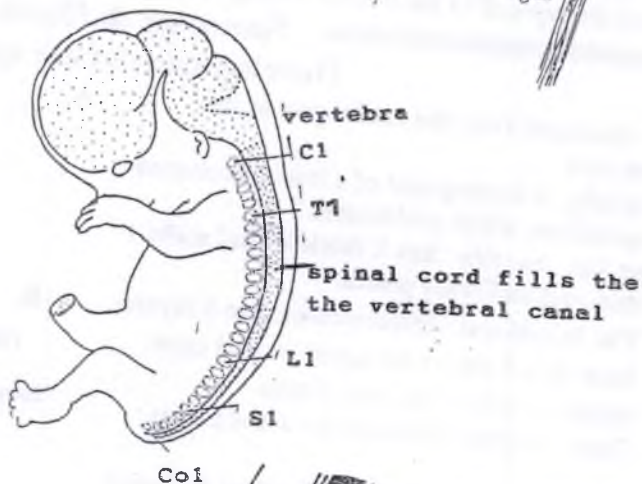
- Ependymal cells, which line the central canal of the spinal cord.
- Neuroblasts which migrate to mantle layer (gray matter) to give → nerve cells (unipolar, bipolar, multipolar)
- Glioblasts which migrate to mantle layer to give → neuroglial cells (astrocytes and oligodendroglia).

N.B. Microglia (mesoglia) are the only cells in the CNS which are mesodermal in origin. They reach the CNS with the invading blood.

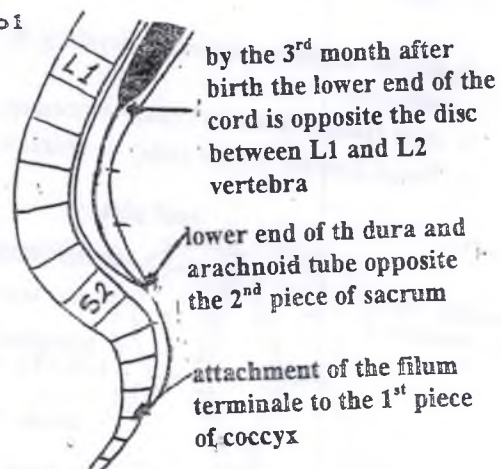


Growth of the spinal cord

A. Till the 3rd month of intrauterine life the spinal cord fills the vertebral canal.



B. At birth its lower end reaches the 3rd lumbar vertebra.



C. By 3rd month after birth it takes its adult position opposite the disc between 1st & 2nd lumbar vertebra.

Development and derivatives of the neural crest

-It arises as a **strip of neuro-ectodermal cells** situated along the lateral edge of the neural plate (one on each side). After fusion of these edges to form the neural tube, the 2 neural crests **separate as 2 longitudinal cords** that **migrate ventrally** to lie one on each side of the tube.

-The neural crest becomes **segmented, migrated** and gives rise to the following derivatives:

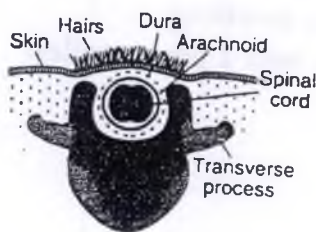
- 1- **Ganglia of certain cranial nerves** (5,7,8,9 and 10th nerves).
- 2- **Dorsal root ganglia** of all spinal nerves.
- 3- **Autonomic ganglia** (sympathetic and parasympathetic).
- 4- **Neurolemmal cells**: responsible for myelination of the peripheral nerves.
- 5- **Medulla of suprarenal gland**: (its cortex is mesodermal in origin).
- 6- **Leptomeninges (Arachnoid and pia mater)**: (the dura is mesodermal in origin).
- 7- **Wandering neural crest cells** which will form the **autonomic tissue** in association with the **digestive system and blood vessels**.
- 8- **Melanoblasts** which differentiate into melanocytes responsible for formation of melanin pigment.
- 9- **Part of pharyngeal arches skeletal element**

N.B. The new experimental evidence showed that the neural crest cells in the head and neck region migrate to the pharyngeal arches.

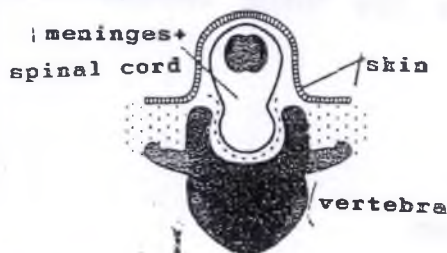
These cells differentiate into the skeletal elements (cartilaginous, membranous) which will ossify and give mandible, palate, maxilla and other structures in the head.

Summary & Illustrations

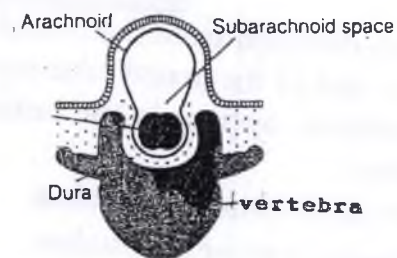
Anomalies of the spinal cord



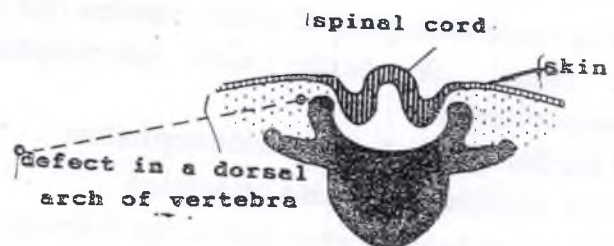
1. **Spina bifida occulta**: due to failure of fusion of the dorsal part of the vertebrae. The vertebrae do not fully enclose the spinal cord.



3. **Meningo-myelocoele**: the meninges and spinal cord bulge through the defect.



2. **Meningocele**: the meninges bulge through the defect.



4. **Myelocoele**: the spinal cord is exposed to the surface through the defect in the vertebral column.

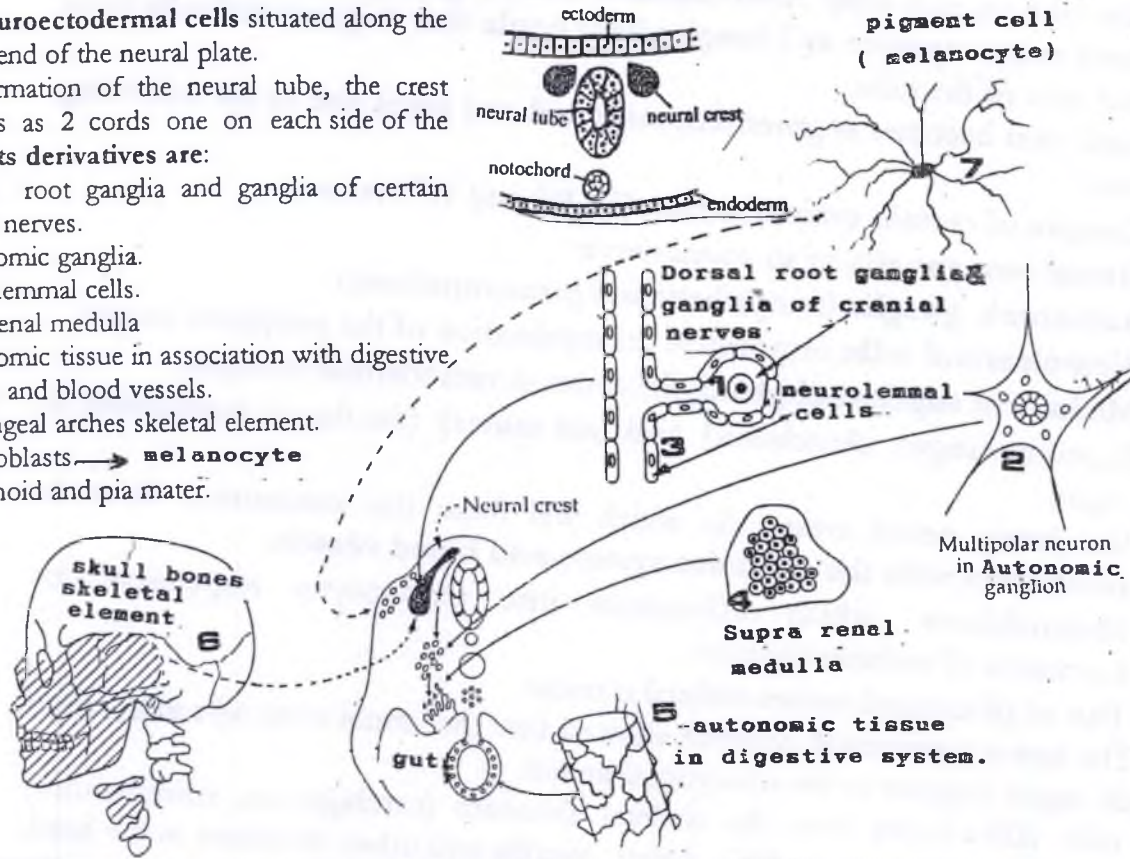
Summary & Illustrations

Development and derivatives of the neural Crest

-It is a **neuroectodermal cells** situated along the lateral end of the neural plate.

-After formation of the neural tube, the crest appears as 2 cords one on each side of the tube. **Its derivatives are:**

1. Dorsal root ganglia and ganglia of certain cranial nerves.
2. Autonomic ganglia.
3. Neurolemmal cells.
4. Suprarenal medulla
5. Autonomic tissue in association with digestive system and blood vessels.
6. Pharyngeal arches skeletal element.
7. Melanoblasts → **melanocyte**
8. Arachnoid and pia mater.



Development of the brain

The brain develops from the cranial end of the neural tube as follows:

The cranial end of the neural tube expands to form the **brain swelling**.

2 constrictions appear in the brain swelling, dividing it into 3 parts: called **brain vesicles**:

- i- forebrain or **prosencephalon**.
- ii- midbrain or **mesencephalon**.
- iii- hindbrain or **rhombencephalon**.

The 3 brain vesicles differentiate as follows:

- The forebrain: gives 2 optic vesicles (the future eyes) then divides into:-
 - i. 2 lateral diverticula called **telencephalic vesicles** (the future cerebral hemispheres).
 - ii. a median part called the **diencephalon**.
- The midbrain: remains undivided.
- The hind brain: gives rise to the following derivatives:
 - i- **metencephalon** which forms the pons & cerebellum.
 - ii- **myelencephalon** which forms the medulla oblongata.

Flexures of the brain:

1. **Cephalic flexure:** This flexure is concave ventrally. The forebrain bends ventrally as a result of formation of head fold.
2. **Pontine flexure:** This flexure is concave dorsally. It occurs in the region of the pons and leads to dilatation of the 4th ventricle.
3. **Cervical flexure:** This flexure is concave ventrally. The hindbrain forms a bent on the spinal cord.

Summary for the derivatives of the brain vesicles

Vesicle	Derivatives	Cavity
telencephalon	cerebral hemispheres	lateral ventricle
diencephalon	thalamus and hypothalamus	third ventricle
mesencephalon	mid brain	cerebral aqueduct
metencephalon	pons and cerebellum	fourth ventricle
myelencephalon	medulla oblongata	

Development of the brain stem

The brain stem consists of **medulla oblongata**, **pons** and **mid brain** (from below upward).

- 1- **Medulla oblongata:** develops from the **myelencephalon**.
- 2- **Pons:** develops from the **metencephalon**.
- 3- **Mid brain:** develops from the **mesencephalon**.

Changes in the Wall of Brain Stem:

-Like the spinal cord the brain stem is formed of 2 lateral walls, thin roof plate and a thin floor plate.

-The lateral wall becomes differentiated into a **ventral basal lamina (plate)** and a **dorsal alar lamina (plate)**, with the **sulcus limitans** separating between them.

-The alar lamina comes to lie lateral to the basal lamina.

-As a result of rotation of the alar lamina in a lateral direction on each side, the roofplate is greatly stretched.

-The **basal lamina** comprises the **motor nuclei**, while the **alar lamina** comprises the **sensory nuclei**. These motor and sensory nuclei are arranged in **longitudinal columns** throughout the whole length of the brain stem.

Columns of the Basal Lamina:

These are 3 **motor (efferent) columns** which are arranged as follows, from medial to lateral:

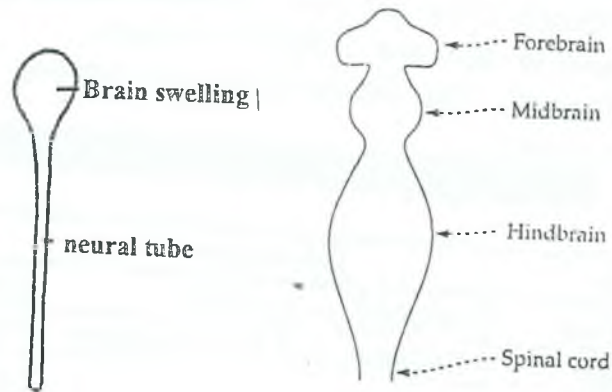
1- Somatic efferent column:

- It gives rise to the **nuclei** which supply somatic muscles (i.e. derived from somites); these nuclei are:

- **12th nucleus:** in the medulla.
- **6th nucleus:** in the pons.
- **3rd and 4th nuclei:** in the midbrain.

Summary & Illustrations Development of the brain

- The brain develops from the cranial end of the neural tube as follows:
- The cranial end of the neural tube expands to form the **brain swelling**.
- 2 constrictions appear in the brain swelling, dividing it into 3 parts: called **brain vesicles**:
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 - iii. hindbrain or **rhombencephalon**.



- The 3 brain vesicles differentiate as follows:

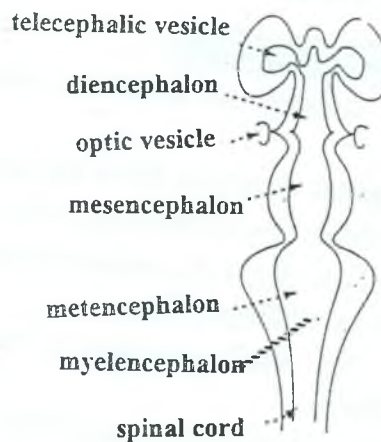
The forebrain: gives 2 optic vesicles (the future eyes) then divides into:

- i. 2 lateral diverticula called **telencephalic vesicles** (the future cerebral hemispheres), &
- ii. A median part called the **diencephalon** (the future thalamus and hypothalamus).

The midbrain: remains undivided.

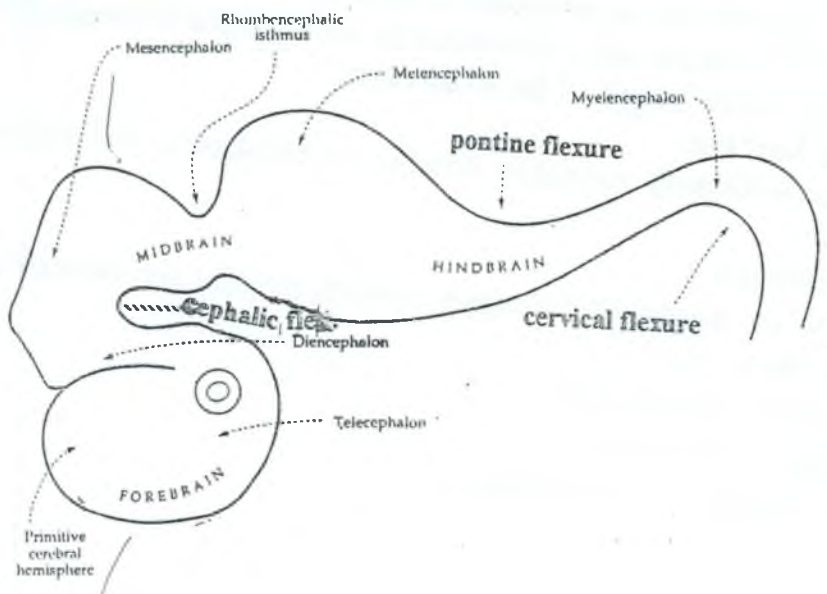
The hind brain: gives rise to:

- i- **metencephalon** which forms the pons & cerebellum.
- myelencephalon** which forms the medulla oblongata.



- 3 flexures appear:

- i. **cephalic flexure:** concave ventrally. The forebrain bends ventrally due to the formation of head fold.
- ii. **pontine flexure:** concave dorsally. Occurs in the region of the pons.
- iii. **cervical flexure:** concave ventrally. Occurs between the hindbrain and spinal cord.



Development of the brain stem (*continued*)

2- Special visceral efferent column:

It gives rise to the **nuclei** which supply muscles derived from the **visceral (pharyngeal) arches**, i.e. **special visceral**.

* These nuclei are the following:

- **5th and 7th motor nuclei**: in the pons.

Nucleus ambiguus in the medulla which gives rise to **9th, 10th and 11th motor nuclei**.

3- General visceral efferent column:

• Its nuclei supply the viscera by autonomic (parasympathetic) fibres. These nuclei are the following:

- **Dorsal nucleus of vagus**: in the medulla oblongata.
- **Inferior salivary nucleus**: in the medulla oblongata (associated with the **9th nerve**).
- **Superior salivary nucleus**: in the pons (associated with the **7th nerve**).
- **Edinger-Westphal nucleus**: in the midbrain (associated with the **3rd nerve**).

Columns of the Alar Lamina:

These are **4 sensory (afferent) columns** which are arranged as follows, from medial to lateral:

1- General visceral afferent column:

• This column is represented by the **sensory component of the dorsal nucleus of the vagus (10th nerve)** which receives sensory fibres (afferents) from the viscera (e.g. lungs and gut).

2- Special visceral afferent column:

• It is represented by the **nucleus of tractus solitarius** which receives taste sensation from the tongue and epiglottis.

3- General somatic afferent column:

- It receives sensory fibres from the skin of the face and scalp as well as proprioceptive sensation from the muscles of mastication and probably muscles of the eyeball and face.
- This column is represented by the **3 sensory nuclei of the trigeminal 5th nerve**: spinal (mainly in the medulla), main sensory (in the pons) and mesencephalic (in the midbrain).

4- Special somatic afferent column:

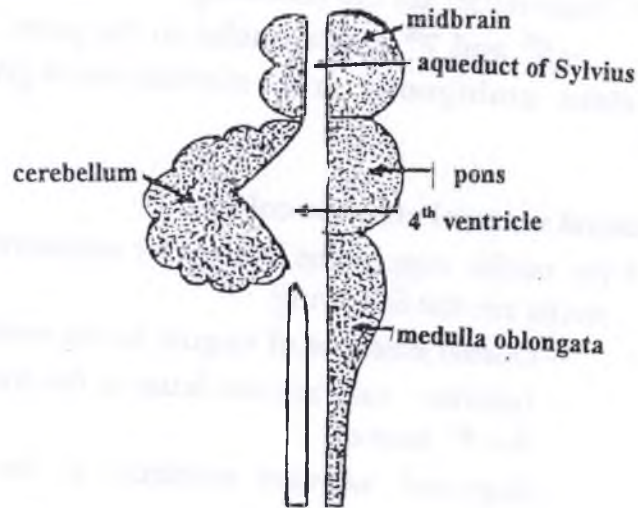
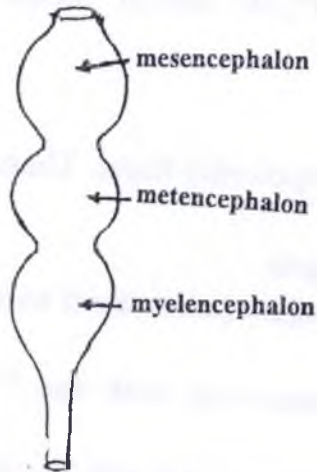
- This column receives the afferent fibres of the auditory (**8th nerve**), and represented by the **cochlear and vestibular nuclei**.

Summary & Illustrations

Development of the brain stem

The brain stem consists of **medulla oblongata**, **pons** and **mid brain** (from below upward).

1. **Medulla oblongata**: develops from the **myelencephalon**.
2. **Pons**: develops from the **metencephalon**.
3. **Mid brain**: develops from the **mesencephalon**.



The brain vesicles which will give the three parts of the brain stem

Changes in the Wall of Brain Stem:

A-Like the spinal cord the brain stem is formed of 2 lateral walls, thin roof plate and a thin floor plate.

-The lateral wall becomes differentiated into a **ventral basal lamina** and a **dorsal alar lamina**, with the **sulcus limitans** separating between them.

B-The alar lamina comes to lie lateral to the basal lamina.

-As a result of rotation of alar lamina on lateral direction on each side, the roof plate is greatly stretched.

-The basal lamina differentiates into 3 motor (efferent) nuclei:

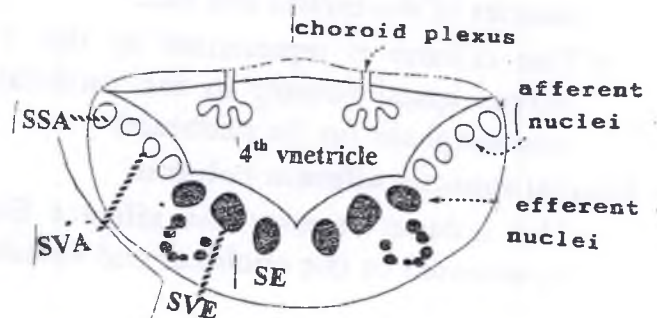
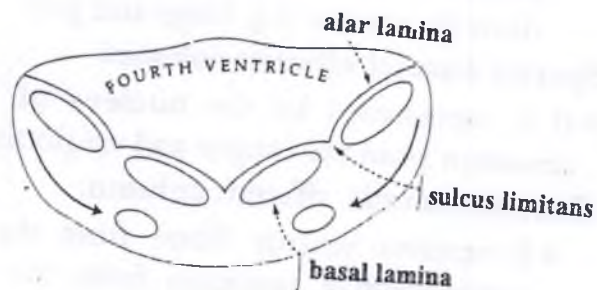
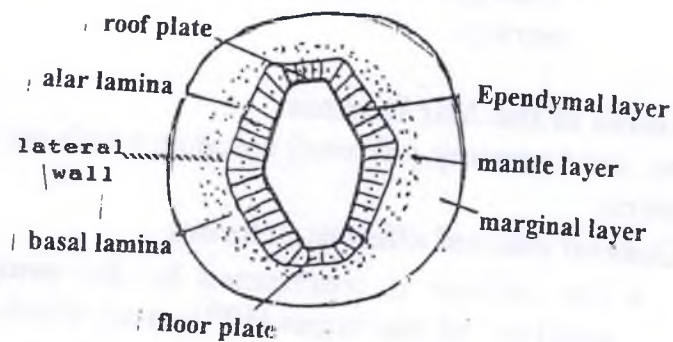
- i. somatic efferent SE
- ii. special visceral efferent SVE
- iii. general visceral efferent GVE

-The alar lamina differentiates into 4 sensory (afferent) nuclei:

- i. general visceral afferent GVA
- ii. special visceral afferent SVA
- iii. general somatic afferent GSA
- iv. special somatic afferent SSA

These motor and sensory nuclei are arranged in longitudinal columns throughout the whole length of the brain stem.

Parts of the brain stem

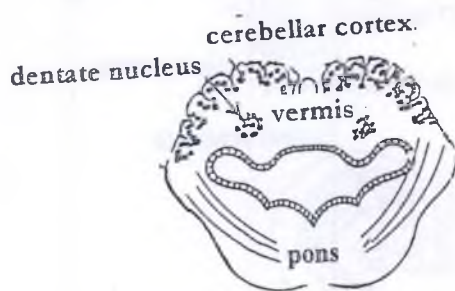


Summary & Illustrations

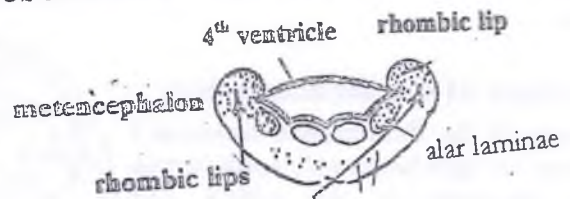
Development of the cerebellum

The cerebellum is formed of the dorsal part of the alar laminae of the metencephalon as follows:

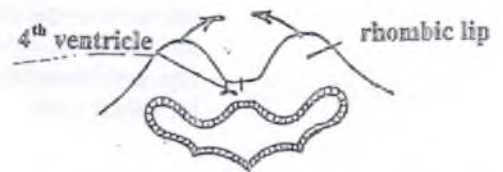
- The alar laminae of both sides bend medially to form the **rhombic lips** each of which grows to form **medial & lateral bulges**.
- The **medial bulges** of both sides meet each other over the roof plate of the 4th ventricle & unite forming the **vermis**.
- The **lateral Bulges** grow to form the cerebellar hemispheres.
- The **cerebellar cortex** is formed by migration of neuroblasts from the mantle layer to enter the marginal layer.
- The **dentate nucleus** develops as a collection of neuroblasts which remains deeply situated in the mantle layer.
- The **cerebellar peduncles** develop later as the axons of the neurones of the cerebellar nuclei grow out of the cerebellum to reach the brain stem.



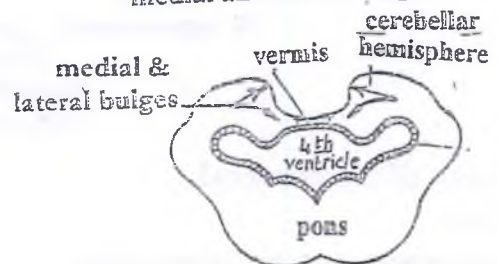
D. Some cells of alar lamina remain deep forming **cerebellar nuclei**. Other cells migrate to the marginal layer forming **cerebellar cortex**.



A. The rhombic lips arise as dorso-lateral extension of the alar lamina



B. The lips grow medially over the roof of 4th ventricle and form medial and lateral bulges

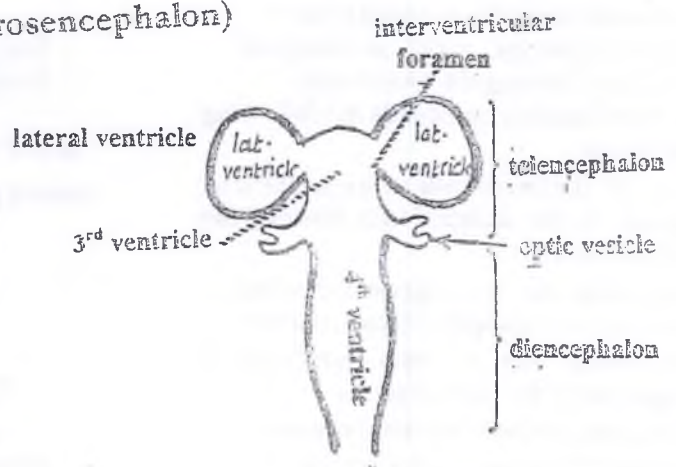


C. The medial bulges meet to form vermis of cerebellum. The lateral bulges form cerebellar hemispheres

Forebrain (prosencephalon)

The forebrain vesicle (prosencephalon). It is the most cranial of the 3 brain vesicles. It gives off a lateral **diverticulum on each side** (optic vesicle). The prosencephalon is **divided into 2 parts**:

1. **Diencephalon**: consists of the posterior part of the prosencephalon (just caudal to the origin of the 2 optic vesicles). It gives rise to the **thalamus, hypothalamus, epithalamus and pineal body**. It encloses a common cavity called 3rd ventricle.
2. **Telencephalon**: consists of the anterior (cranial) part of the prosencephalon together with the 2 optic vesicles. The telencephalon gives 2 lateral outpocketings forming the cerebral hemispheres.



Summary & Illustrations

-Each hemisphere has a cavity called lateral ventricle.

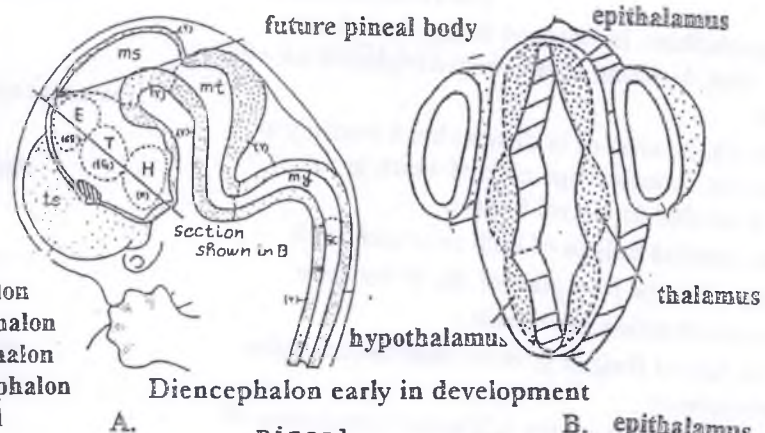
-Each optic vesicle will give the retina and optic nerve.

Development of the diencephalon:

- The walls of the diencephalon thicken as 3 swellings in each lateral wall: **epithalamus** above, **thalamus** in the middle and **hypothalamus** below.

- At first, the **epithalamus** is relatively large but it decreases in size later.

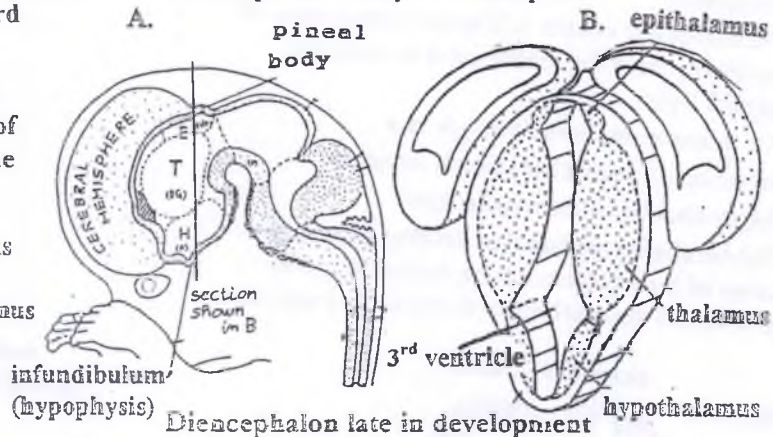
te: telencephalon
ms: mesencephalon
mt: metencephalon
my: myelencephalon
sc: spinal cord



Diencephalon early in development

- The **thalamus** and **hypothalamus** enlarge.
- The **pineal body** develops from the roof and the **hypophysis** develops from the floor of the diencephalon.

E: epithalamus
T: thalamus
H: hypothalamus



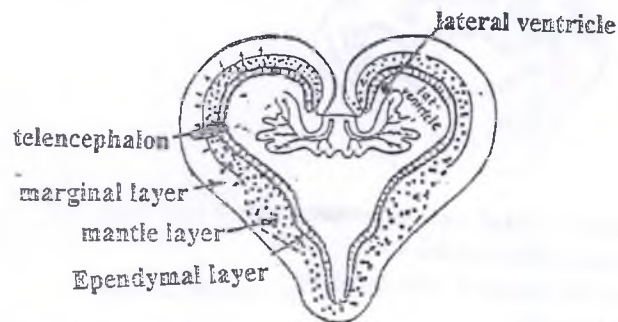
Diencephalon late in development

Development of the cerebral hemispheres

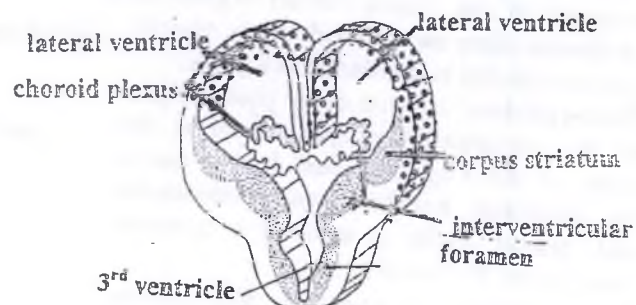
- The 2 hemispheres arise as 2 evaginations (telencephalon) from the lateral wall of the forebrain (prosencephalon).
- The cavity of each hemisphere is the lateral ventricle.
- The wall of the telencephalon is formed of 3 layers: i. **ependymal** (lining the cavity of the lateral ventricle), ii. **mantle** (nerve cells forming the grey mater), iii. **Marginal** (nerve fibres forming the white mater).

As the development proceeds the following changes occur:

- Most of the nerve cells in the mantle layer migrate to the marginal layer forming the cerebral cortex.
- Some cells do not migrate and remain to form the basal ganglia (corpus striatum).
- The medial wall of each hemisphere is invaginated by the choroid plexus.
- Each lateral ventricle becomes separated from the 3rd ventricle except for the interventricular foramen.



Early in development, the wall of telencephalon formed of ependymal, mantle & marginal layer

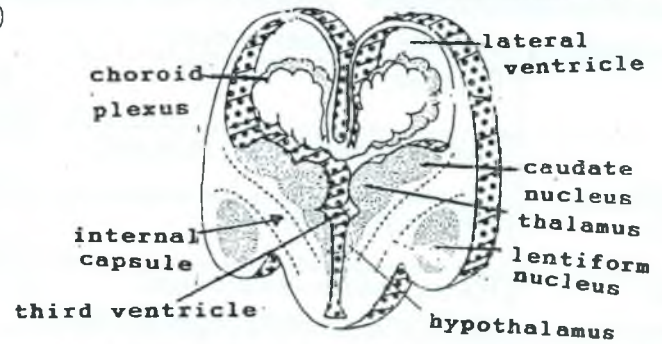


Most of the cells migrate forming cerebral cortex
Some cells remain forming the basal ganglia

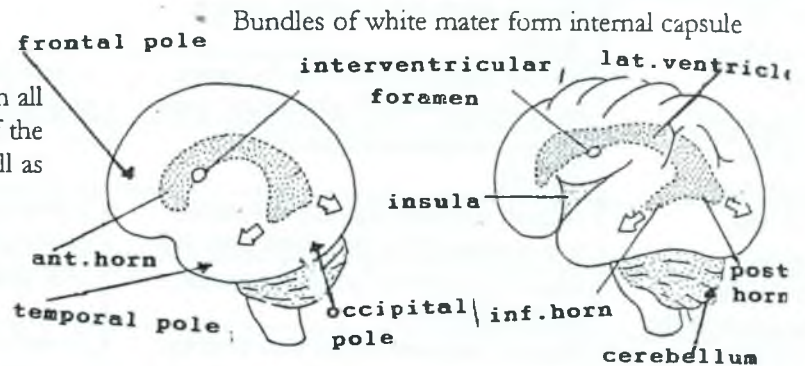
Summary & Illustrations

Development of the cerebral hemisphere (continued)

- The axon of the nerve cells (neuroblasts) invades the wall of the cerebral hemisphere forming the white mater.
- Bundles of the white mater also separate between the thalamus, caudate and lentiform nuclei forming the internal capsule.



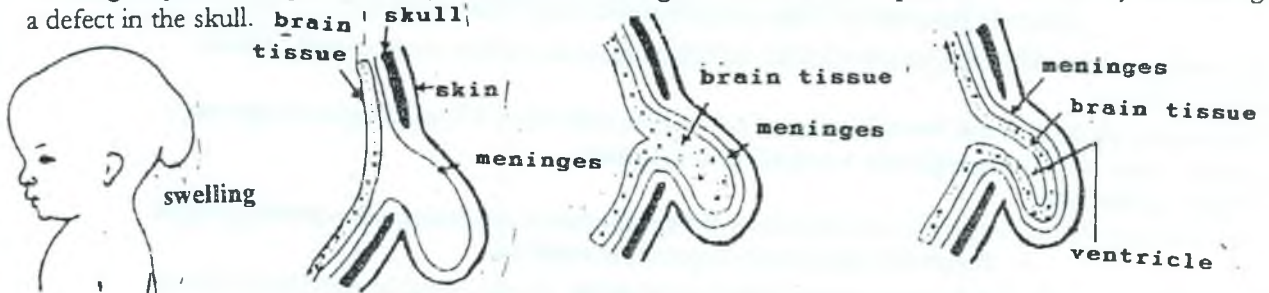
- Expansion of the cerebral hemisphere in all directions resulting in the formation of the poles, and fissures of the cerebrum as well as the horns of the lateral ventricle.



The cerebrum expands in all directions forming the poles and fissures of cerebrum

Commonest anomalies

1. **Hydrocephalus**, marked enlargement of the skull due to distention of the ventricles in the brain.
2. **Anencephaly**, severe arrest in the development of the cerebral hemisphere.
3. **Microcephaly**, marked diminution in the size of the skull due to diminution in the size of the brain.
4. **Meningocele**, protrusion of the meninges through a defect in the skull.
5. **Meningo-encephalocele**, protrusion of the meninges + part of brain tissue through a defect in the skull.
6. **Meningo-hydro-encephalocele**, protrusion of meninges + brain tissue + part of ventricular system through a defect in the skull.



Swelling protruded through a defect in the skull! A. Meningocele B. Meningo-encephalocele C. Meningo-hydro-encephalocele

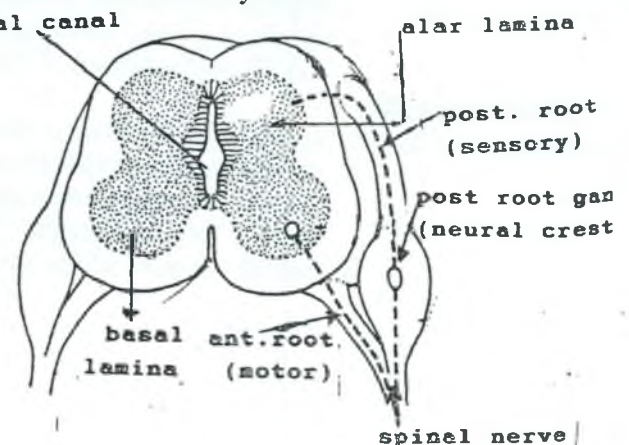
Development of the peripheral nervous system

A. Development of spinal nerves:

Each spinal nerve is formed by union of 2 roots:
i. anterior root (motor) & ii. posterior root (sensory).

-The anterior root develops from the axons of motor cells in the basal lamina (anterior horn) of spinal cord.

-The posterior root develops from the central processes of axons of the cells of posterior root ganglia which are derived from the neural crest (the peripheral processes of the axons of these cells join the anterior root to form the trunk of the spinal nerve).



Summary & Illustrations

B. Development of the cranial nerves

Nerve	Function	Its sensory fibres derived from	Its motor fibres derived from
CN I Olfactory	Sensory, mediates smell (olfaction)	Olfactory (nasal) placode	----
CN II Optic	Sensory, mediates vision	Ganglion cells of retina	----
CN III Oculomotor	Motor, mediates ocular motility, pupillary constriction & accommodation	----	Basal lamina of cranial part of mid-brain
CN IV Trochlear	Motor, innervates superior oblique muscle	----	Basal lamina of caudal part of mid-brain
CN V Trigeminal	Mixed, mediates the sensory, motor innervation of the 1 st pharyngeal arch	Cranial part of neural crest	Basal lamina of cranial part of the pons
CN VI Abducent	Motor, mediates abduction of the eye ball	----	Basal lamina of caudal part of the pons
CN VII Facial	Mixed, mediates sensory and motor innervation of the 2 nd pharyngeal arch	Cranial part of neural crest	Basal lamina of the pons
CN VIII Stato-acoustic	Sensory, mediates hearing, balance and equilibrium	Otic placode	----
CN IX Glossopharyngeal	Mixed, mediates motor and sensory innervation of the 3 rd pharyngeal arch	Cranial part of neural crest	Basal lamina of the medulla
CN X Vagus	Mixed, mediates sensory and motor innervation of the 4 th and 6 th arches	Cranial part of neural crest	Basal lamina of the medulla
CN XI Spinal accessory	Motor, innervates sternomastoid and trapezius.	----	Basal lamina of the spinal segments C1-C6
CN XII Hypoglossal	Motor, innervates the intrinsic and extrinsic muscles of the tongue	----	Basal lamina of the medulla

Development of the autonomic nervous system

A. Development of the sympathetic system (thoraco-lumbar or adrenergic system)

It is derived from

1. Visceromotor cells of the basal lamina of the neural tube from T1 to L3 spinal segments.

This will give rise to the preganglionic sympathetic neurones.

2. Neural crest cells

This will give rise to:

- i. postganglionic neurons of the sympathetic trunk and para-aortic ganglia.
- ii. chromaffin cells of the suprarenal medulla.

B. Development of the parasympathetic system (cranio-sacral or cholinergic system)

It is derived from

1. Visceromotor cells of the basal lamina of the neural tube

This will give rise to:

- i. preganglionic neurons of the parasympathetic nuclei of the spinal cord (S2-S4).
- ii. the preganglionic parasympathetic neurons of medulla CN IX, X, pons CN VII and mid brain CNIII.

2. Neural crest cells

This will give rise to:

- i. postganglionic neurons of the parasympathetic ganglia of body cavities.
- ii. postganglionic neurons of the cranial parasympathetic ganglia, ciliary CN III, pterygopalatine and submandibular CN VII, otic CN IX and terminal or mural ganglia CN X.
- iii. form the neurons of the enteric ganglia.

DEVELOPMENT OF THE SPECIAL SENSE ORGANS

Development of the eye

Optic vesicle:

- It is a bilateral diverticulum of the forebrain at the level of the diencephalon.
- It is connected to the diencephalon by the optic stalk.
- Each vesicle induces the overlying surface ectoderm to thicken and form the lens placode.
- Next the optic vesicle and lens placode invaginate.
- The optic vesicle transformed into double walled optic cup.
- The 2 layers of the optic cup form the retina. The inner layer forms the nervous layers, the outer layer forms the retinal pigmented epithelium.
- The optic stalk is invaginated inferiorly by the choroid fissure which contains the hyaloid artery.
- The optic stalk forms the optic nerve and the hyaloid artery becomes the central retinal artery.

Lens:

- Derived from the ectoderm overlying the optic vesicle.
- The ectoderm forms a thickening called lens placode.
- This becomes invaginated to form the lens pit.
- The pit is closed to form the lens vesicle.
- The epithelial cells on the posterior part of the vesicle give the lens fibers.

Cornea:

- Anteriorly the stratified epithelium of the cornea is ectodermal in origin.
- The deeper layers derived from the mesenchyme which surrounds the optic cup and stalk.

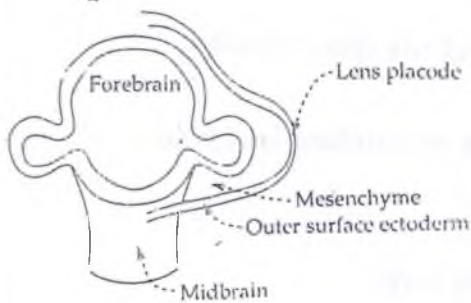
Sclera and choroid:

- They are derived from mesenchyme which surrounds the optic cups and stalk.
- The mesenchyme condenses into 2 layers (outer and inner).
- The outer layer forms the sclera and the deeper layer of the cornea. This layer is continuous with the dura matter.
- The inner layer forms the choroid which is continuous with the pia and arachnoid meninges.

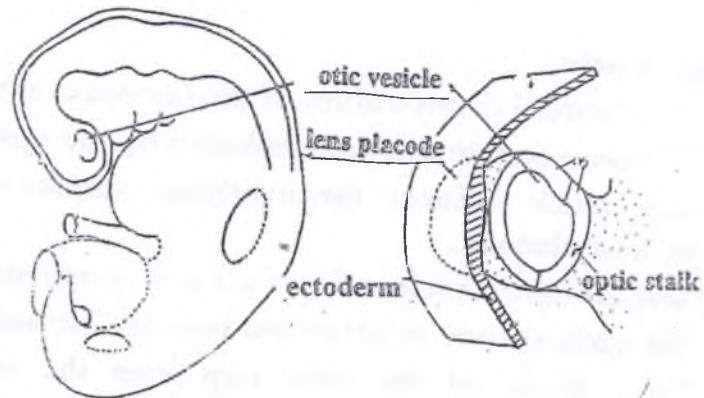
Summary & Illustrations

Development of the special sense organs

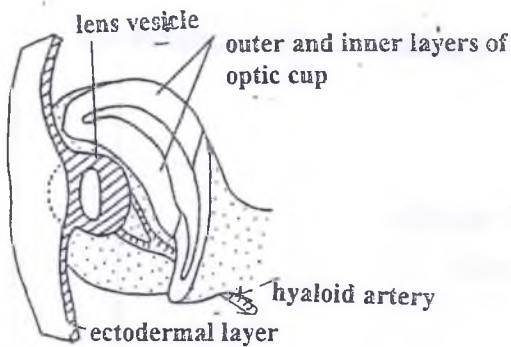
Development of the eye



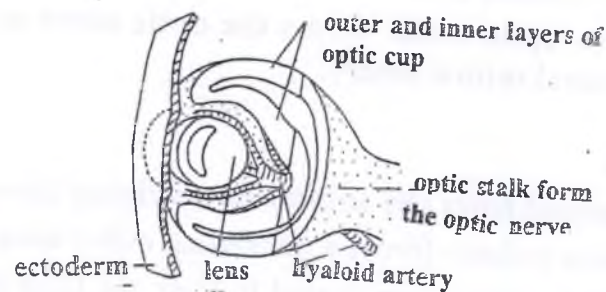
A. The optic vesicle is a bilateral diverticulum of the fore brain



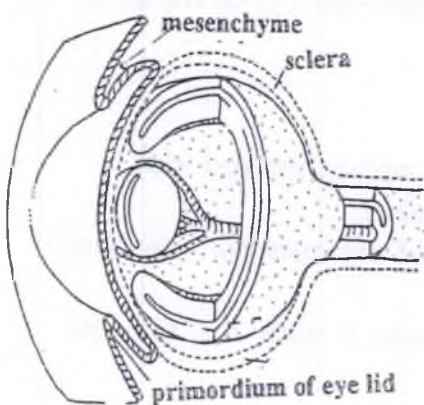
B. The optic vesicle stimulates the surface ectoderm to form lens placode. The optic stalk connects the optic vesicle to the diencephalon



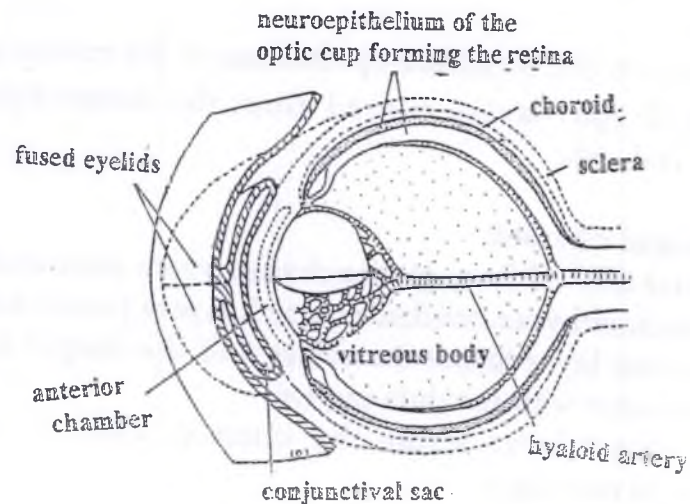
C. The lens placode is transformed to a lens vesicle.
-The optic vesicle becomes optic cup
-Optic stalk is invaginated by choroid fissure which contains hyaloid artery



D. The lens vesicle separates from the ectoderm and is transformed into lens.
-The 2 layers of the optic cup → retina



E. The eyelids develop as 2 folds from the ectoderm which covers the cornea. The folds are invaginated by the covering mesenchyme



F. The sclera and choroid develop from the mesenchyme which surrounds the optic cup.
-The vitreous body develops from the mesenchyme which fills the optic cup.

A. Iris and ciliary body:

- The **epithelium** of the iris, ciliary body, sphincter and dilator pupillae muscles are **neuroectodermal in origin**. They are derived as an extension from the neuroepithelium of the anterior part of optic cup.
- The **pigmented epithelium** of iris arises from migrating cells of **neural crest**.
- The **connective tissue** and **ciliary muscles** arise from the **mesenchyme** around the optic cup.

The vitreous body & anterior and posterior chambers of the eye:

- The **vitreous body** arises from the **mesenchyme** which fills the optic cup.
- The anterior and posterior chambers are separate aqueous chambers which develop in the mesenchyme which covers the eye.
- The **anterior chamber** lies between the developing **iris and cornea**.
- The **posterior chamber** lies between the developing **iris and lens**.

Eye lids:

- Develop as 2 **ectodermal folds** which cover the cornea and **invaginated by the surrounding mesenchyme**.
- The upper and lower folds **fuse together in the third month**.
- **Separate in the seventh month**.
- The **conjunctival sac** lines the two eye lid folds, so it is **ectodermal in origin**.

Lacrimal sac and nasolacrimal duct:

- Appear as a **cellular ingrowth** from the cleft between the **frontonasal process and the maxillary process** during the development of the face.
- This ingrowth is later canalized.

Development of the Ear

The ear is divided into 3 major regions, internal, middle and external ear.

The internal ear

- In the week 4, the surface ectoderm thickens to form **otic placode** which is found near the region of the hindbrain.
- The otic placode then invaginates to form an **otic pit**.
- As the otic pit loses its connection with the surface ectoderm, the edges of the pit fuse to form the **otic vesicle** (otocyte).
- The otic vesicle is the primordium of the **membranous labyrinth**.

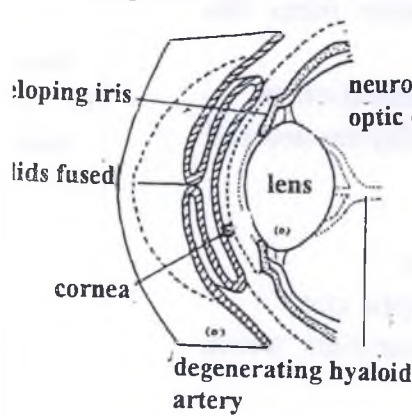
Development of the membranous labyrinth:

A tubular diverticulum from the otic vesicle develops and later forms the endolymphatic duct and sac.

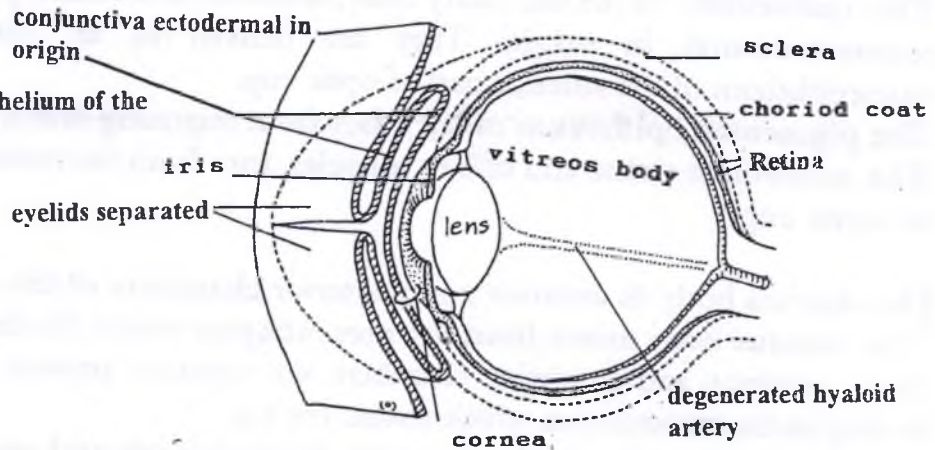
- The otic vesicle becomes constricted near its middle to form 2 major regions:
A. Dorsal utricular portion and B. Ventral saccular portion.

Summary & Illustrations

Development of the eye (continued)



G. The epithelium of the iris, ciliary body & pupillae muscle arise as extension from neuroepithelium of optic cup.
-The pigmented epithelium of the iris arises from the neural crest

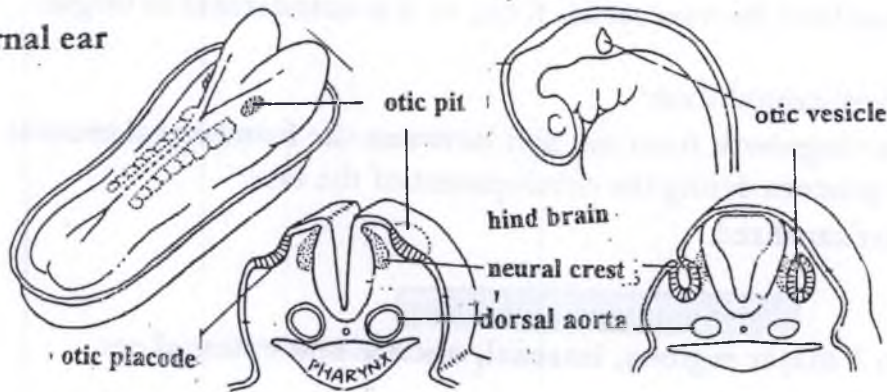


H. The epithelium of the cornea is ectodermal in origin
-The deeper layers derive from the surrounding mesenchyme.
-The proximal part of the hyaloid artery becomes the central retinal artery.
-The distal part inside the vitreous body degenerates

Development of the ear

The ear is divided into **internal, middle and external ear.**

The internal ear



Otic placode (thickened epithelium) → **otic pit** → **otic vesicle** which is the primordium of **membranous labyrinth**.

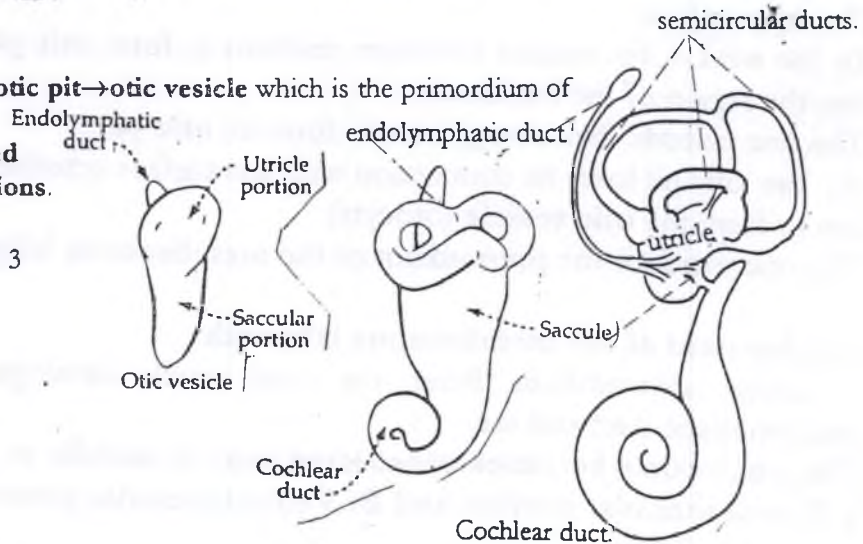
The **otic vesicle** constricts to be divided into: **A. utricular** and **B. saccular portions**.

The **utricular portion** gives:

- i. utricle, ii. endolymphatic duct & the 3 semicircular ducts.

The **saccular portion** gives:

- i. Saccule and
- ii. Cochlear duct.



Development of the internal ear (*continued*)

The utricular portion gives:

- i. The utricle, ii. the endolymphatic duct and iii. the 3 semicircular ducts.

The saccular portion gives rise to the i. saccule and ii. cochlear duct.

The cochlear duct spirals to form the cochlea and the spiral organ of Corti, differentiates in its wall.

The middle ear

The endoderm of the 1st pharyngeal pouch extends and expands to form the tubotympanic recess.

The recess envelops the auditory ossicles.

The tubotympanic recess gives the epithelial lining the tympanic cavity, mastoid atrum, mastoid air cells and auditory tube.

The **tympanic membrane** forms where the recess contacts the ectoderm of the 1st pharyngeal cleft.

The mastoid process is not present at birth, and the facial nerve is exposed.

The mastoid process develops around the 2nd year.

Contents of the middle ear:

a- Ossicles of the middle ear:

1- Malleus and incus: derived from the cartilage of the 1st branchial arch.

2- Stapes: derived from the cartilage of the 2nd branchial arch.

b- Muscles in the middle ear:

1- Tensor tympani: from the 1st arch (supplied by the mandibular nerve).

Stapedius: from the 2nd arch (supplied by the facial nerve).

The external ear

It is formed of auricle and external acoustic meatus.

The auricle develops from the 6 auricular (swellings) hillocks around the dorsal end of the 1st pharyngeal cleft. The hillocks are produced by proliferation of mesenchyme from the 1st and 2nd pharyngeal arches.

The hillocks fuse to form the auricle.

The external acoustic meatus develops from the ectoderm of the 1st pharyngeal cleft.

Commonest anomalies

1. Absence of auricle (due to failure of formation of auricular hillocks)
2. Deformed auricle (due to faulty modeling of the auricular hillocks)
3. Abnormal small auricles
4. Abnormal large auricles
5. Congenital deafness (due to maternal infection with rubella)

Summary & Illustrations

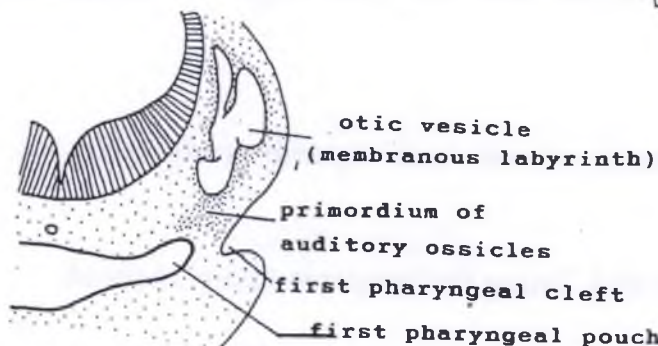
Development of the ear (continued)

The middle ear:

The 1st pouch gives the auditory tube and the tympanic cavity. The cavity envelops the auditory ossicles (malleus, incus and stapes).

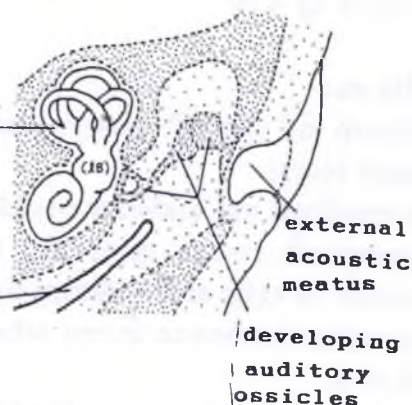
A.

WEEK 6



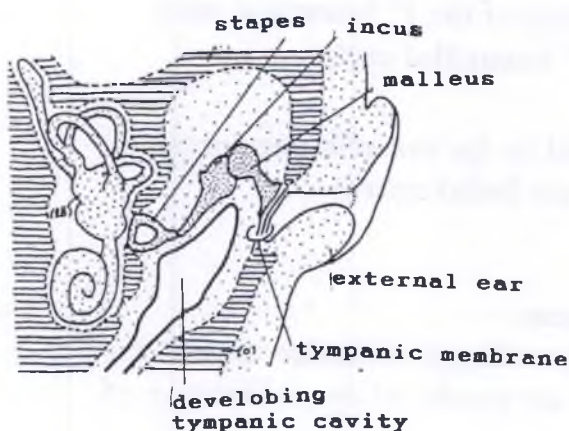
B.

WEEK 10



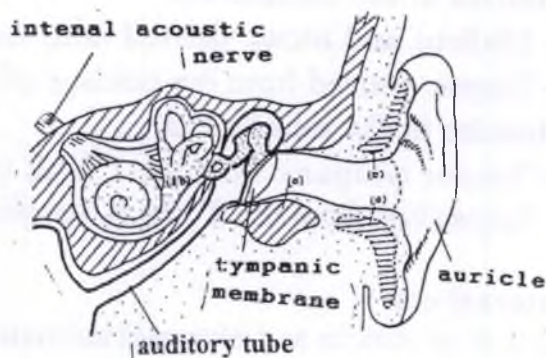
C.

WEEK 21



D.

AFTER BIRTH

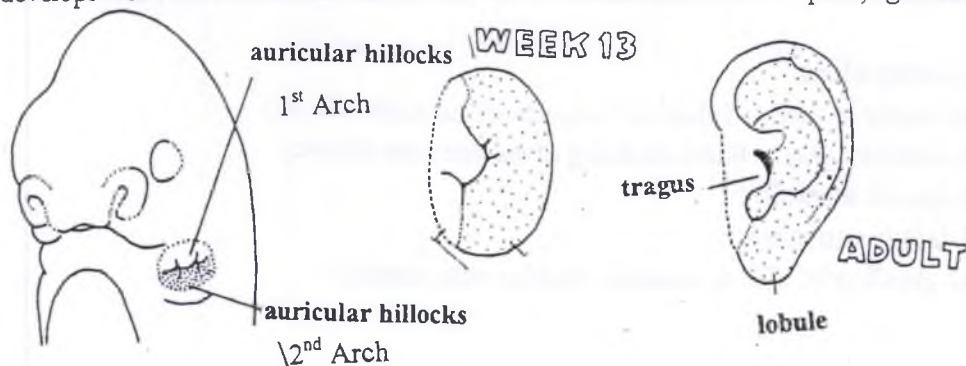


The external ear:

-It is formed of: i. external acoustic meatus & ii. The auricle

-The external acoustic meatus: derives from the 1st pharyngeal cleft.

-The auricle develops from the 6 auricular hillocks around the dorsal end of the 1st pharyngeal cleft.



DEVELOPMENT OF THE SKELETAL AND MUSCULAR SYSTEMS

Development of the vertebral column

- The vertebral column develops from sclerotomes of the mesodermal somites.
- The sclerotomes surround the notochord. They form segments called protovertebrae.
- Each protovertebra is composed of a light cranial part & a dense caudal part.
- The dense caudal part of a protovertebra fuses with the light cranial part of the protovertebra caudal to it, forming a blastemal vertebra. This is composed of mesodermal tissue which chondrified and later ossified.
- The fused mass forms the centrum of the vertebra which is chondrified from 2 centres of chondrification.
- The dorsal process (laminae) as well as costal, lateral processes arise as extensions from the centrum.
- The 2 dorsal processes surround the neural tube and fuse together posteriorly in the midline to form the dorsal arch and the spine.
- The fate of the costal and transverse processes differ in the different regions of the vertebral column as follows:
 - i. In the cervical region: they unite and form the foramen transversum of the vertebral artery.
 - ii. In the thoracic region: they extend ventrally to form the ribs.
 - iii. In the lumbar region: the 2 elements remain fused, the costal element forming the anterior part of the transverse process.
 - iv. In the sacrum: the 2 parts remain fused and form the lateral mass of sacrum.
- The intervertebral discs develop in the interval between the light and dense parts of the protovertebra (i.e. in the middle zone of sclerotome).
- The notochord disappears in the regions where the vertebra develops. However, in the region where the discs develop the notochord persists to form the nuclei pulposus of the discs.
- *The intervertebral disc develops from the middle zone of the sclerotome (i.e. segmental in position). Its nucleus pulposus is derived from the notochord, while the annulus fibrosus is derived from the surrounding mesoderm.

Commonest anomalies

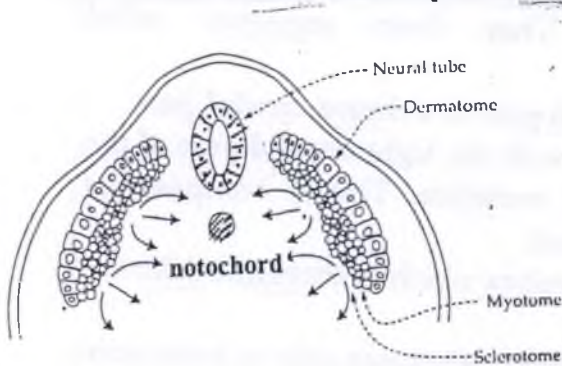
1. **Spina bifida** It is a failure of fusion of the dorsal processes of the vertebrae. It usually affects the lumbar and sacral regions. It is of several types:
 - a. **Spinal bifida occulta**: There is a defect in the dorsal arch of the vertebra. The cord and meninges are directly covered by hairy skin (illustrations on page 78).
 - b. **Meningocele**: The meninges bulge out of the defect in the dorsal arch of the vertebra.
 - c. **Meningomyelocele**: The spinal cord and meninges protrude through the defect.
 - d. **Myelocele**: The neural tissue exposed to the surface through the defect (illustration on page 78).
2. **Sacralization of the 5th lumbar vertebra**: i.e. fusion of the 5th lumbar vertebra with the 1st piece of sacrum.
3. **Lumbarization of the 1st sacral vertebra**: i.e. separation of the 1st piece of sacrum to form a separate vertebra.

Summary & Illustrations

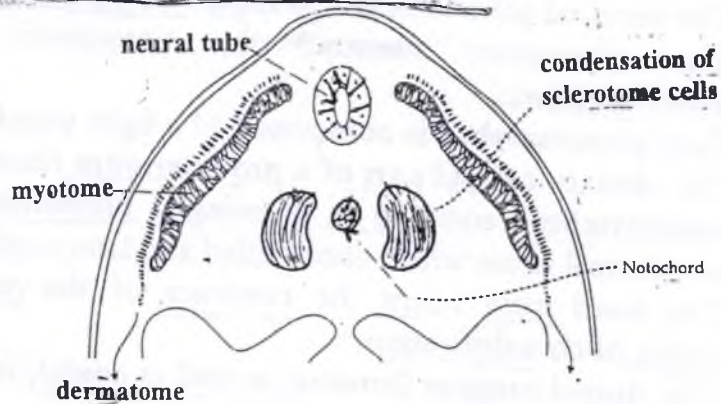
DEVELOPMENT OF THE SKELETAL AND MUSCULAR SYSTEMS

Development of the vertebral column

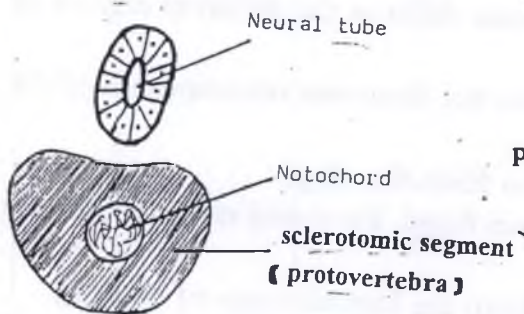
The vertebral column is developed from the sclerotomes of mesodermal somites.



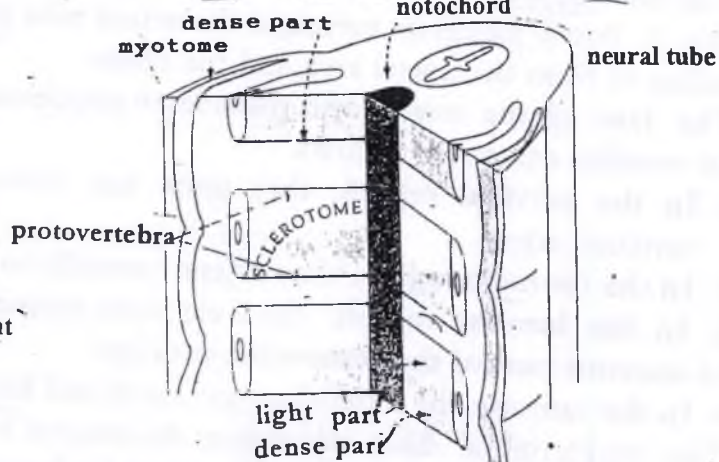
A. The sclerotomic cells of the mesodermal somites migrate to surround the notochord



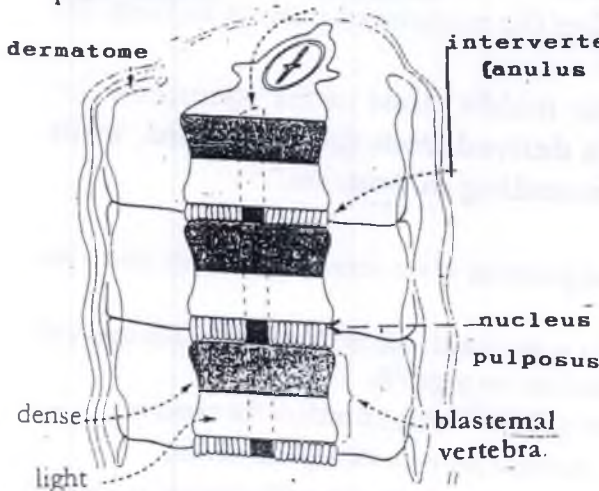
B. the cells condense to surround the notochord



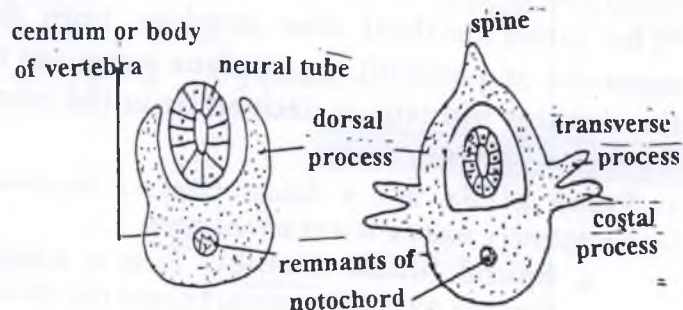
C. The cellular condensation forms the protovertebra. , notochord



D. Each protovertebra is composed of light cranial part and dense caudal part.



E. The dense caudal part of the protovertebra above fuses with the light cranial part of the protovertebra below to form the blastemal vertebra.



F. Each blastemal vertebra gives 3 processes (dorsal, costal & transverse)
The dorsal process encircles the neural tube
Forming the dorsal arch and spine.

Supernumerary vertebrae - increase in number of vertebrae in certain region

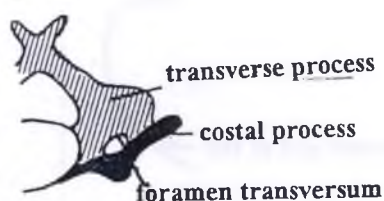
Commonest anomalies (continued)

4. **Kyphosis**: A prominent increased backward convexity of a part of the vertebra.
5. **Kypho-scoliosis**: Combination of kyphosis and scoliosis.
6. **Supernumerary vertebrae**: It is an increase in the number of vertebrae in certain region.
7. **Missed vertebrae**: It is a decreased number of certain vertebrae due to error in sclerotomic segmentation.

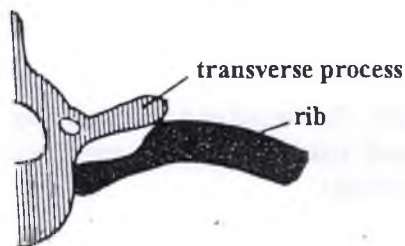
Summary & Illustrations

Development of the vertebral column (continued)

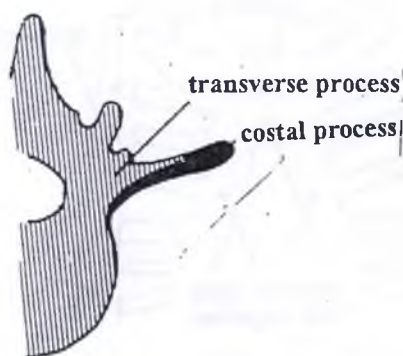
Fate of the dorsal and transverse processes of the blastemal vertebra



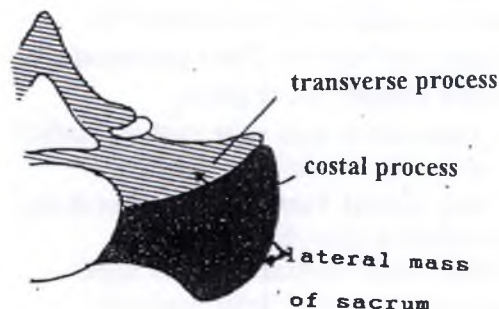
A. In the cervical region the 2 processes unite and encircle the foramen transversum of vertebral artery



B. In the thoracic region, the costal processes extend ventrally and form the ribs.



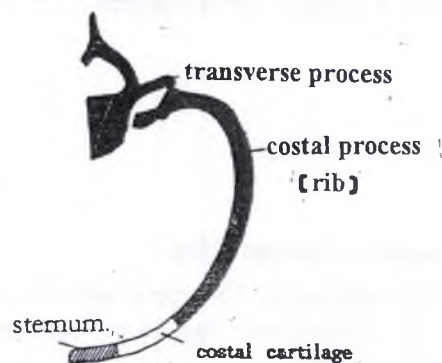
C. In the lumbar region the costal processes form the anterior part of the transverse process of the vertebra



D. In the sacral region, the 2 processes fuse to form the lateral mass of sacrum.

Development of the ribs

- Ribs develop from the costal processes of the thoracic vertebrae.
- They begin as mesodermal condensation, then undergo chondrification.
- Each rib is ossified except for its ventral (sternal part) which persists as a costal cartilage.
- The upper seven pairs of ribs form the true ribs because their cartilages remain attached to the sternum.
- The lower five ribs are known as false ribs because their cartilages do not reach the sternum.



The rib develops as a ventral extension from the costal process of the thoracic vertebra.

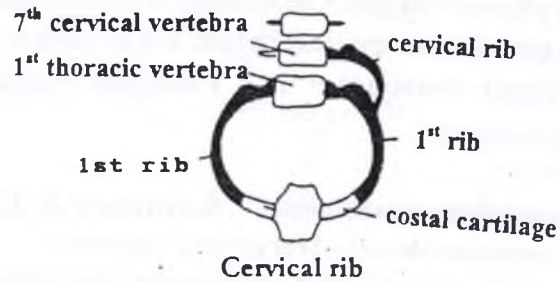
Summary & Illustrations

Commonest anomalies

1. Supernumerary rib: It may develop in relation to 7th cervical vertebra (**cervical rib**) or 1st lumbar (**lumbar rib**).

The cervical rib if present may **press on the subclavian artery and the lower trunk of brachial plexus**.

2. Forked rib: The sternal end of the rib may be bifurcated and attached to the sternum by a pair of costal cartilages.



forked anterior end of the rib

Forked rib

Development of the sternum

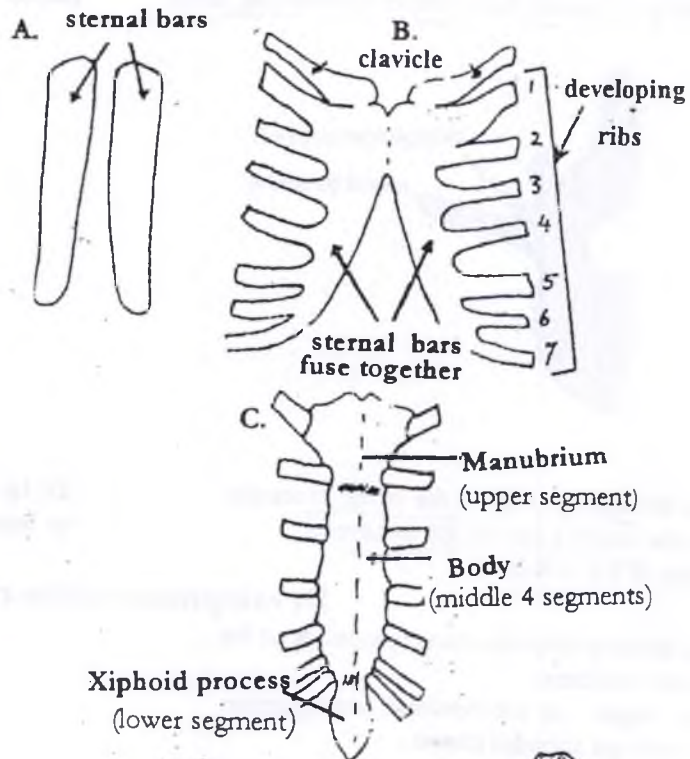
- Develops as a **mesodermal condensation**, on each side, which joins the ends of the developing ribs together. These condensations are called **sternal bars** or plates.

- The lateral side of each plate joins the medial ends of clavicle and the upper 7 ribs.

- The two **sternal bars fuse together** in the median plane to form the sternum.

Chondrification and ossification of the fused plates lead to formation of sternal segments which form **the 3 parts of sternum**:

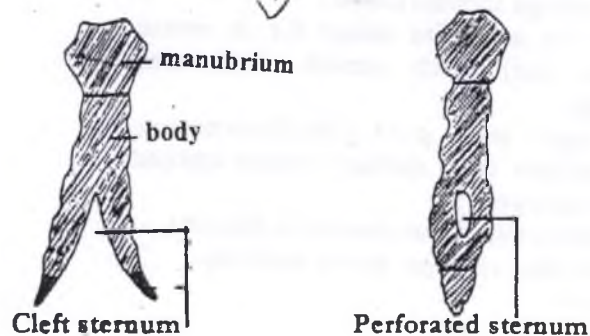
- i. **Manubrium** sterni (upper segment).
- ii. **Body** of sternum (middle 4 segments).
- iii. **Xiphoid process** (lower segment).



Commonest anomalies

1. Cleft sternum: The upper or lower parts of the 2 sternal bars may fail to fuse leading to cleft sternum.

2. Perforated sternum: Localized failure of fusion of the 2 sternal bars may lead to development of foramen in the sternum.



Development of the skull (Cranium)

-The skull develops from the mesoderm surrounding the developing brain.

-Developmentally it is divided into 2 parts:

I. Neurocranium which forms the brain box.

II. Viscerocranium which forms the facial skeleton.

I. Neurocranium: It is divided into:

A. Skull cap (membranous neurocranium):

It is formed of the frontal bone, parietal bone, interparietal part of occipital bone, squamous part of temporal bone, nasal bone and lacrimal bones. These bones ossify membrane (membranous ossification).

B. Skull base (chondrocranium or cartilaginous neurocranium):

It ossifies in cartilage (cartilaginous ossification). It is developed from several parts.

-Close to the middle line 4 pairs of medial cartilages:

i. Inter-orbitonasal cartilage (trabecula cranii) lies between the orbit and nasal cavity. It is represented by the ethmoid bone.

ii. Hypophyseal cartilage: in relation to hypophysis cerebri. It is represented by the sphenoid bone which lodges the hypophyseal fossa.

iii. Parachordal (basal) plate:

A part which surrounds the most cranial part of the notochord. It extends cranially till the level of the hypophysis. It forms the base of the occipital bone.

iv. Occipital sclerotomes: 4 in number close to the notochord, they fuse to form part of the occipital bone.

More laterally 3 paired cartilages arranged antero-posteriorly:

1. Ala orbitalis → the primordium of the lesser wing of sphenoid.

2. Ala temporalis → the primordium of the greater wing of sphenoid.

3. Otic capsules:

each side of the parachordal plate. Each capsule surrounds the otocyst to petrous and mastoid parts of temporal bone.

Alae fuse with each other forming the base of the skull (ethmoid, base of occipital, petrous temporal) which later ossify.

For the passages of cranial nerves.

Viscerocranium

Bones of the face. It is formed of pharyngeal arches (mainly the 1st two).

Formation of bones of the face is derived from neural crest cells.

Viscerocranium

pharyngeal arch and includes the maxilla, zygomatic bone, bones, palatine, vomer, and mandible.

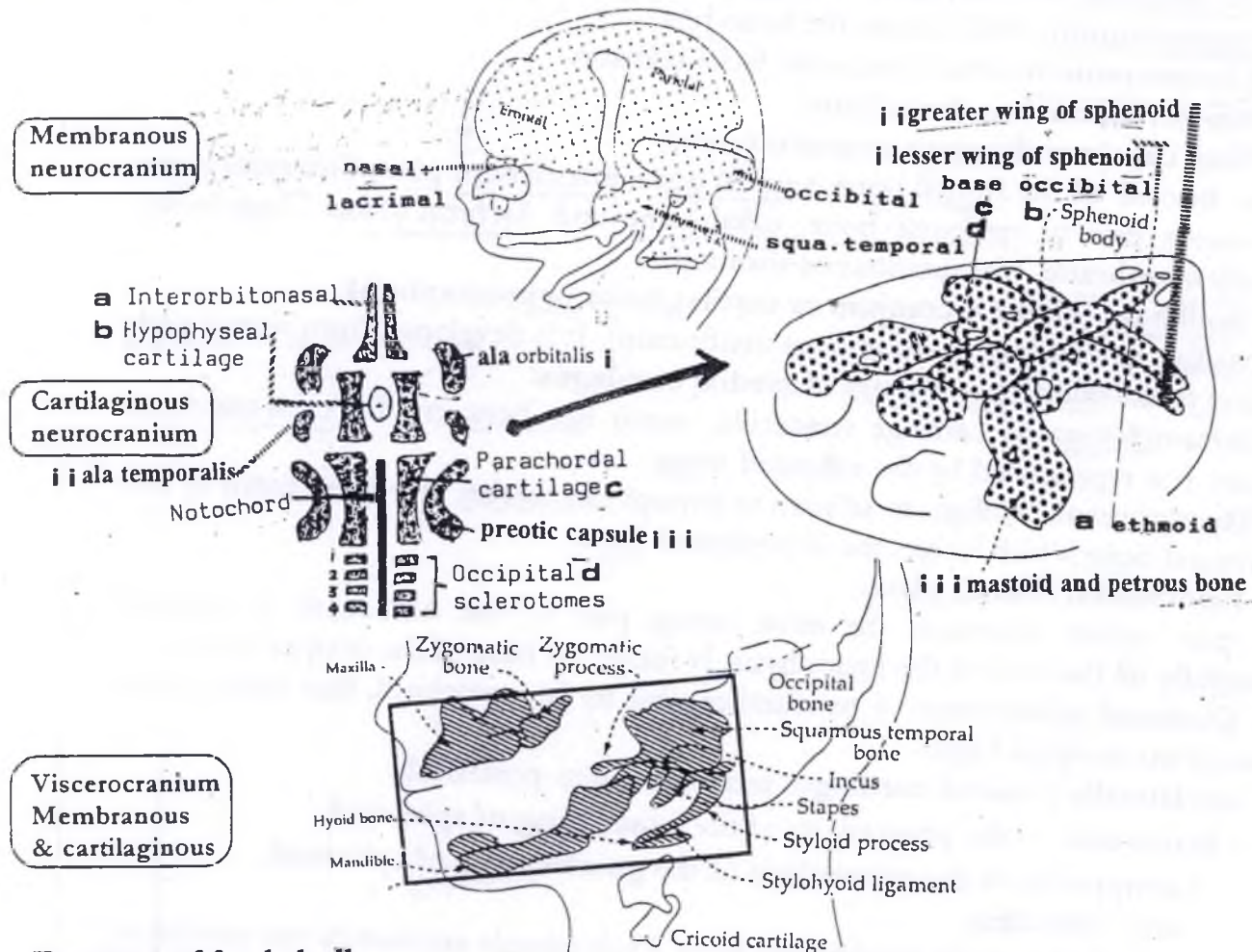
Neurocranium

Pharyngeal arches:

Geniomandibular ligament, spine of sphenoid and Meckel's 1st pharyngeal arch.

Stylohyoid ligament, lesser horn and upper 1/2 of mandible from the 2nd arch.

Summary & Illustrations Development of the skull

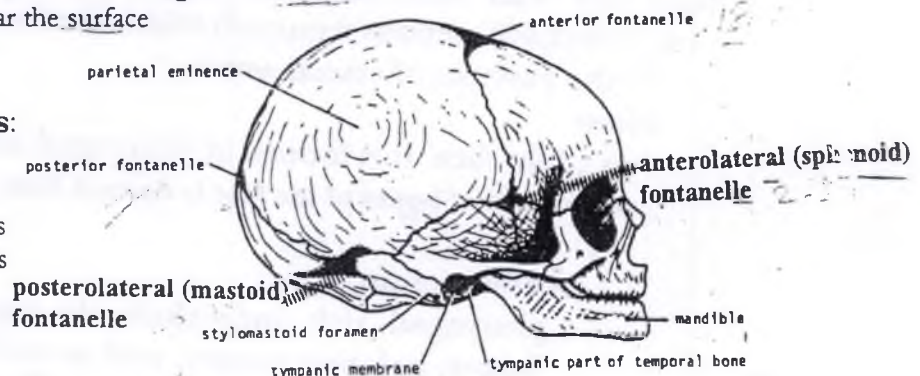


Features of fetal skull:

- The nasal sinuses, teeth, mastoid process, facial canal are not developed
- The lower margin of the orbit lies at the lower margin of the nose:
- The tympanic membrane is very near the surface
- The facial nerve is exposed.

New-born skull fontanelles:

- Anterior closes at 18 months
- Posterior closes at 12 months
- Antero-lateral closes at 2-3 months
- Postero-lateral closes at 12 months

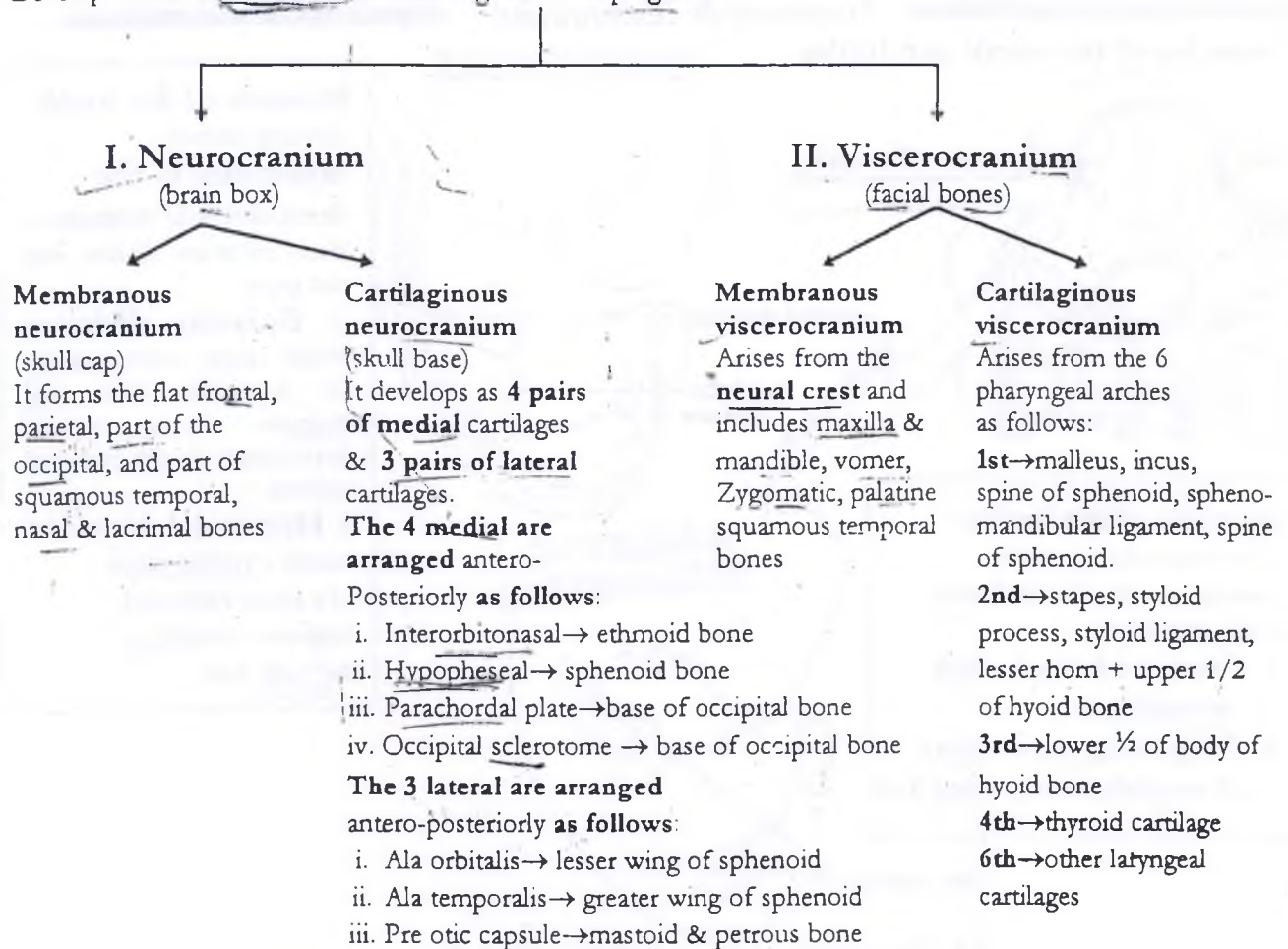


Development of the skull (continued)

- Greater horn and the lower half of the body of the hyoid arise from the 3rd arch.
- Laryngeal cartilages including the thyroid, cricoid, arytenoid, corniculate and cuneiform cartilages arise from the 4th and 6th arches.

Summary for the development of skull (cranium)

Develops from the mesoderm surrounding the developing brain.



Summary & Illustrations

Development of muscles

I. Striated muscle

Muscles of the head and neck

A. Muscles derived from pharyngeal arches:

Muscles of mastication: develop from the 1st pharyngeal arch.

Muscles of the face: develop from the 2nd pharyngeal arch.

Stylopharyngeus m.: develop from the third arch.

Cricothyroid m.: develops from the fourth arch.

Other muscles of larynx: develop from the sixth arch.

B. Muscles of eye ball:

Develop from the preotic myotome.

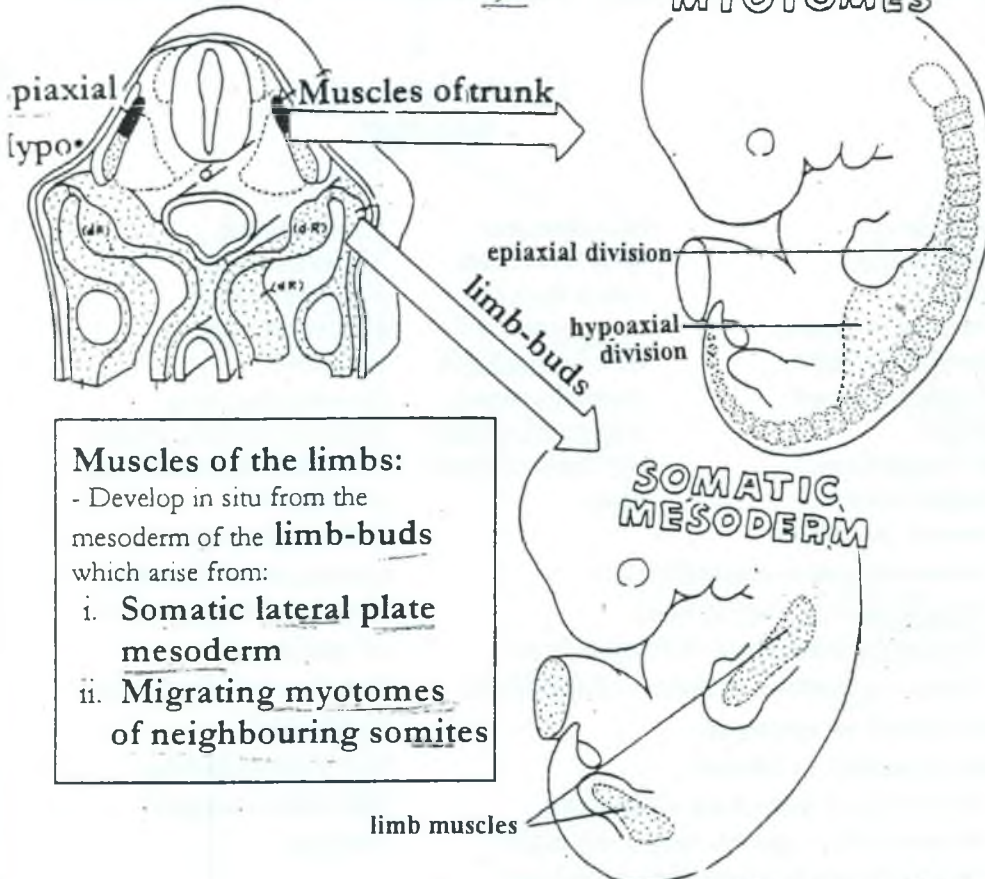
C. Muscles of tongue:

Develop from the occipital myotomes.



Summary & Illustrations

Muscles of the trunk and limbs



Muscles of the trunk:

Develop from the **myotomes of the mesodermal somites**. Each myotome divides into two parts:

1. **Epiaxial division:** which carries a dorsal ramus of a spinal nerve and migrates to a position dorsolateral to the vertebral column.

2. **Hypoaxial division:** carries a ventral ramus of a spinal nerve and migrates ventrally in the body wall.

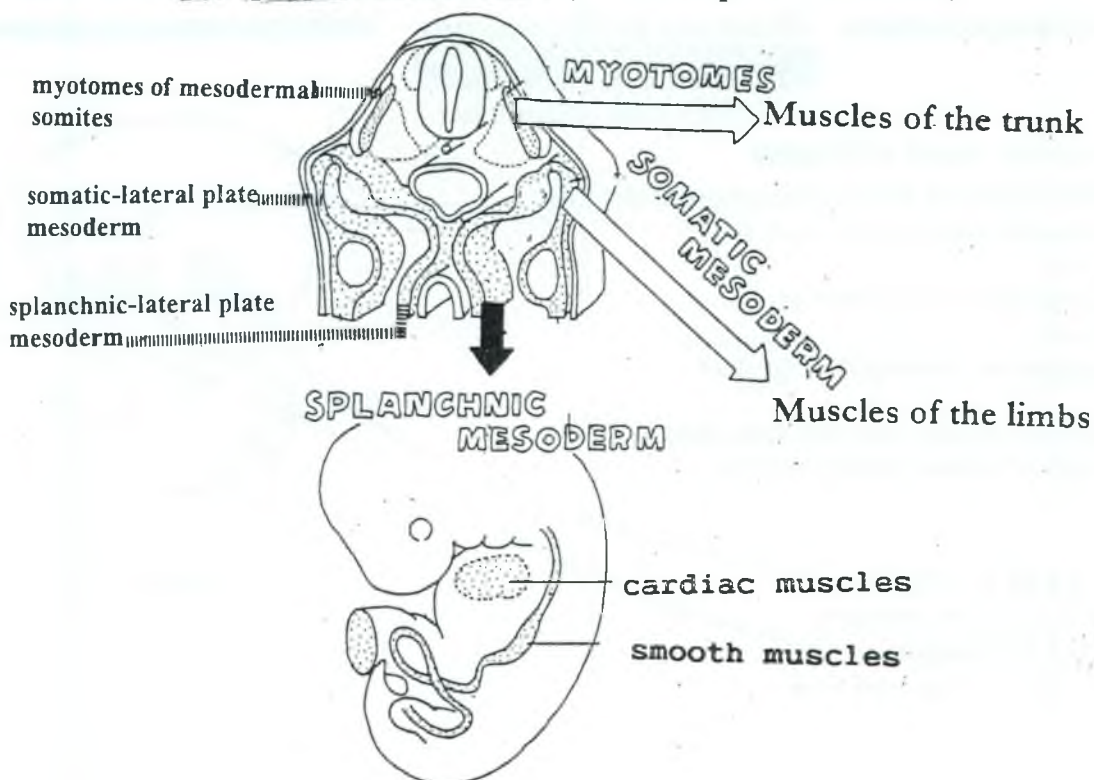
Muscles of the limbs:

- Develop in situ from the mesoderm of the **limb-buds** which arise from:

- i. **Somatic lateral plate mesoderm**
- ii. **Migrating myotomes of neighbouring somites**

II. Smooth and cardiac muscles

Both derive from the splanchnic mesoderm (i.e. lateral plate mesoderm)



Summary & Illustrations

More detail about the origin of smooth muscles:



-The **splanchnic mesoderm** gives → the smooth muscles surrounding the gut and its derivatives.

-However, there are smooth muscles of **ectodermal origin**:

- i. Sphincter and dilator pupillae.
- ii. Myoepithelial cells.

Development of joints

-There are 3 types of joints: fibrous, cartilaginous and synovial.

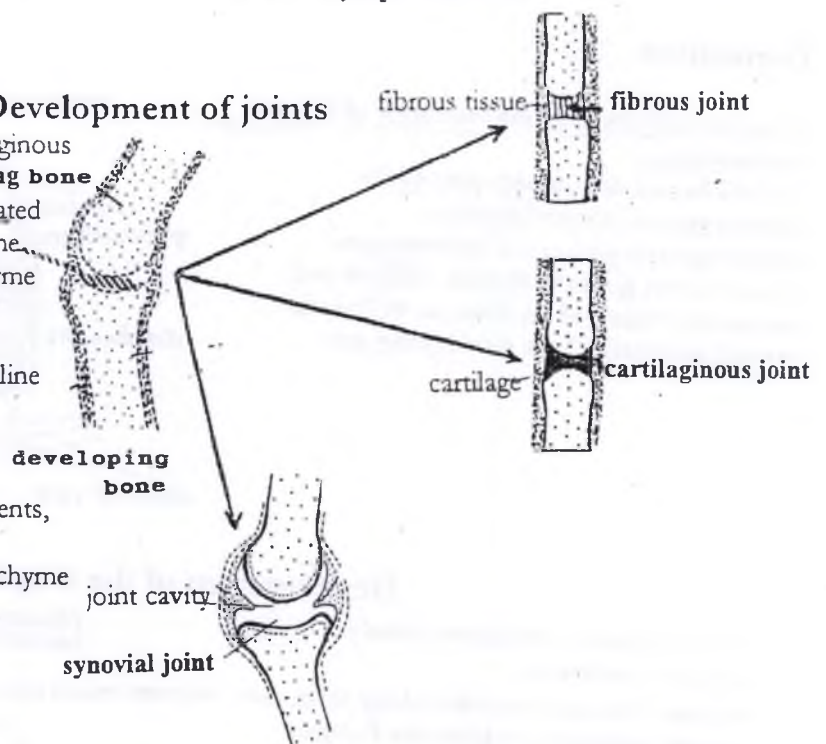
-As adjacent bones develop, they are separated from one another by interzonal mesenchyme.

-In **fibrous joints** the interzonal mesenchyme becomes fibrous tissue.

-In **cartilaginous joints**, the interzonal mesenchyme becomes fibrocartilage or hyaline cartilage.

-In **synovial joints**:

- i. The peripheral part of the interzonal mesenchyme becomes the capsule & ligaments, synovial membrane.
- ii. The central part of the interzonal mesenchyme disappears leaving a joint cavity.

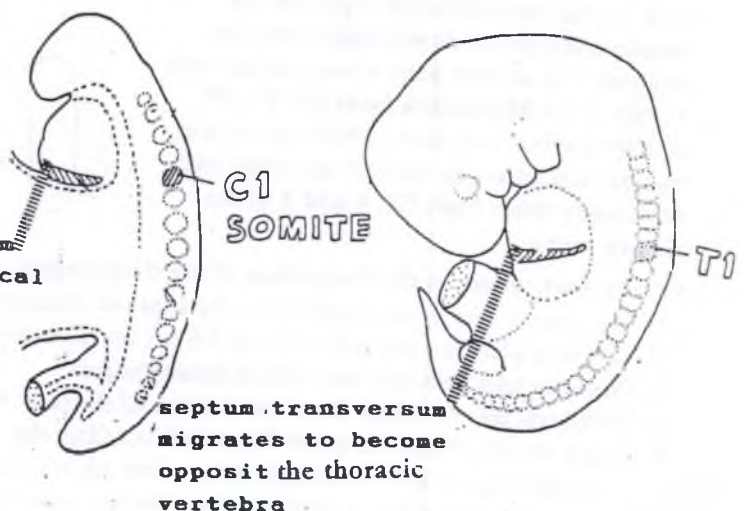


The septum transversum

-A mass of mesoderm formed in the neck in front of **cervical 3, 4, 5 somites**.

-Developing muscle cells (myoblasts) from C3,4,5 myotomes migrate into the septum transversum carrying their nerve supply with them.

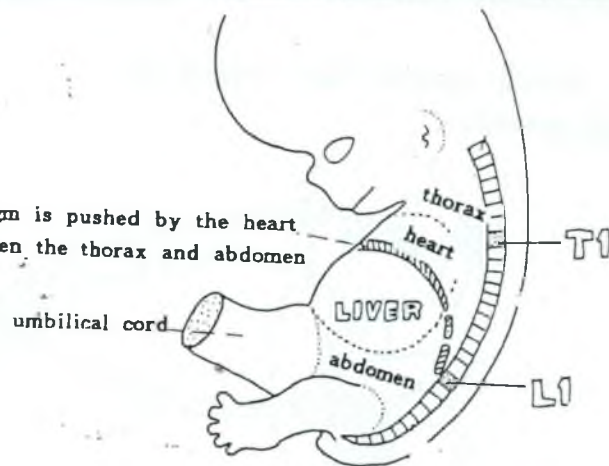
septum transversum
opposit the cervical
vertebra



Summary & Illustrations

-After folding of the embryo, and due to the **descent of the heart**, the septum transversum is pushed caudally (with its motor nerve supply, C3,4,5, i.e. phrenic nerve) to reach its final position separating the thoracic cavity from the abdominal cavity.

the diaphragm is pushed by the heart to lie between the thorax and abdomen

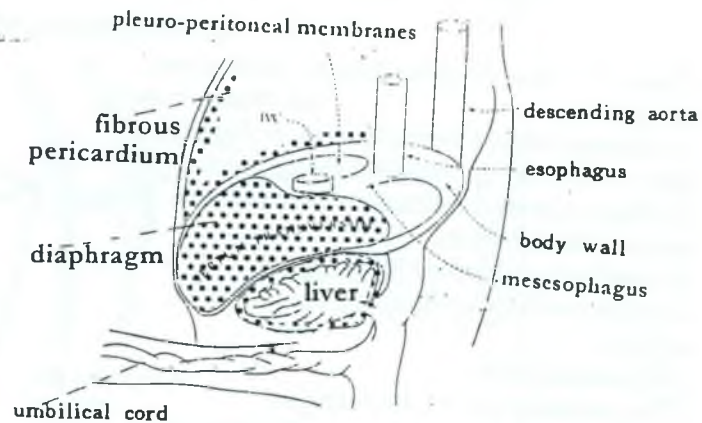


Derivatives

-Its upper part shares in the formation of **fibrous pericardium**.

-Its middle part gives major part of the **diaphragm** and **central tendon**, **diaphragmatic pleura** and **peritoneum**.

-Its lower part gives the **fibrous capsule** and **connective tissue** of the **liver**, as well as the **ventral mesentery** of the developing gut.



Development of the diaphragm

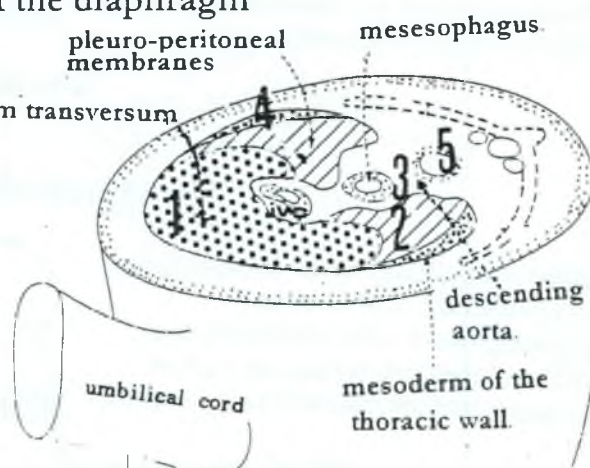
- The diaphragm is developed mainly from the septum transversum.
- A mass of mesoderm extending from the septum transversum ventral abdominal wall to the foregut.
- At first the septum transversum lies in the neck. As the heart descends it pushes the septum transversum downwards to its final position. The septum transversum carries with it parts of the Myotomes from the 3rd, 4th and 5th cervical somites: Invade the septum transversum during its descent and carry with them nerve fibres from C3, 4 and 5 of the phrenic nerve.

- Several parts share in the formation of the diaphragm:

- 1) The greater part is developed from the septum transversum.
- 2) The dorso-lateral parts are developed from the pleuro-peritoneal membranes.
- 3) Posterior part develops from the mesesophagus.
- 4) Peripheral part develops from mesoderm of thoracic wall. Is added to the circumference of diaphragm.
- 5) Crura: develop from the mesoderm surrounding the descending aorta.

NB. ii. The diaphragm receives multiple innervation since it has multiple origin.

ii. The phrenic nerve supplies its abdominal surface as a result of folding of the embryo.



Summary & Illustrations

Congenital anomalies of diaphragm:

1. **Diaphragmatic hernia of Bochdalek:** due to a defect in the pleuro-peritoneal membrane allowing the abdominal viscera to enter the pleural cavity. They close the pleuro-peritoneal communications (one on each side) and lie **dorsolateral to the septum transversum**.
2. **Diaphragmatic hernia of Morgagni:** due to a gap between the sternal and costal origins of the diaphragm.
3. **Hiatus hernia:** due to a wide esophageal hiatus. Which leads to protrusion of the stomach into the thorax.

Development of the Limbs

- Appear as buds (limb-buds) at the beginning of second month.

Each limb bud is formed of a **mass of mesoderm** covered by **glove of ectoderm**. The mesoderm is derived from **2 sources**:

- i. **Lateral plate mesoderm.**
- ii. **Migrated myotomes** from neighboring somites.

- The limb buds elongate and become segmented.

- The upper limb-bud shows segmentation into arm, forearm and hand.

- The lower limb-bud shows segmentation into thigh, leg and foot.

- The ventral rami of spinal nerves from C.4 to T.2 pass into the upper limb-bud.

- The ventral rami of spinal nerves from T.12 to S.4 pass into the lower limb-bud.

- The axial mesoderm of the bud is condensed to form the skeleton of the limb.

- The surrounding mesoderm forms the muscles of the limb.

Rotation of the limb-buds:

- The limb-buds at first form right angles with the trunk.

- Each limb-bud has two borders:

a- preaxial border (cranially) which is marked by the thumb or the big toe.

b- postaxial border (caudally) which is marked by the little finger or little toe.

- The limb-buds undergo a process of adduction and rotation.

- The upper limb rotates laterally, as a result:

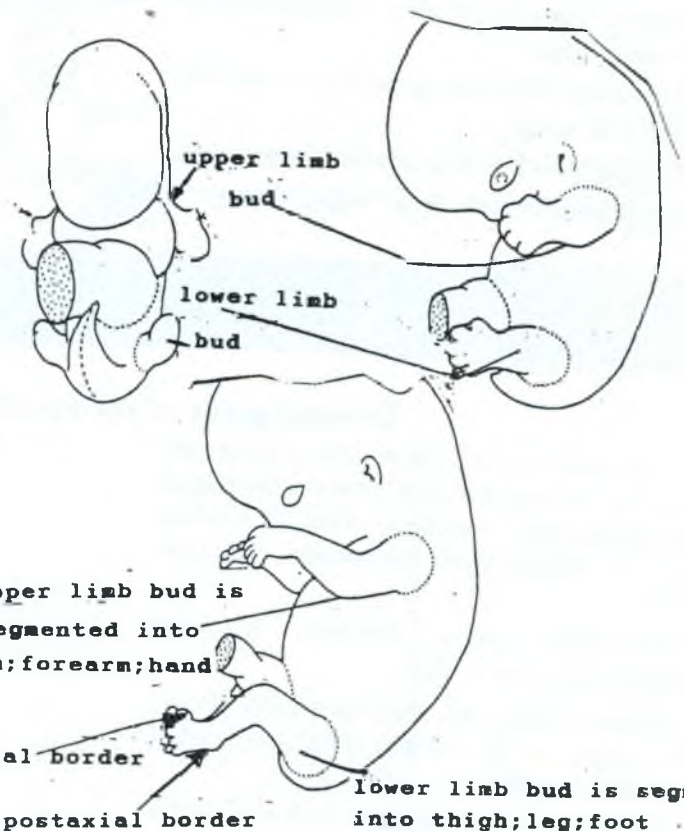
a- The preaxial border becomes lateral.

b- The radius (preaxial bone of forearm) becomes lateral.

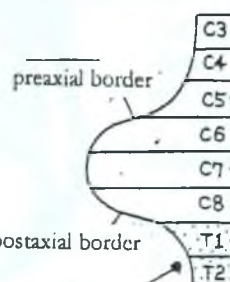
c- Thumb (preaxial finger) becomes lateral.

d- Flexor surface becomes anterior.

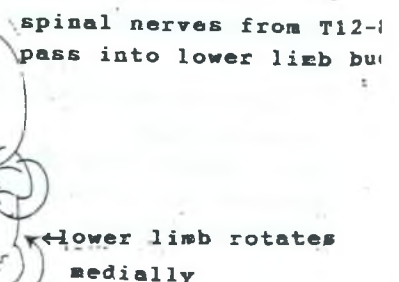
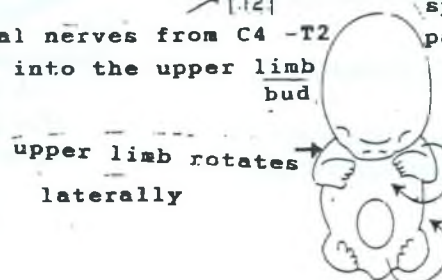
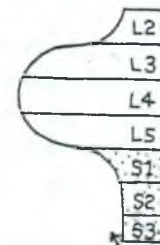
- The lower limb rotates medially, as a result:



UPPER LIMB



LOWER LIMB



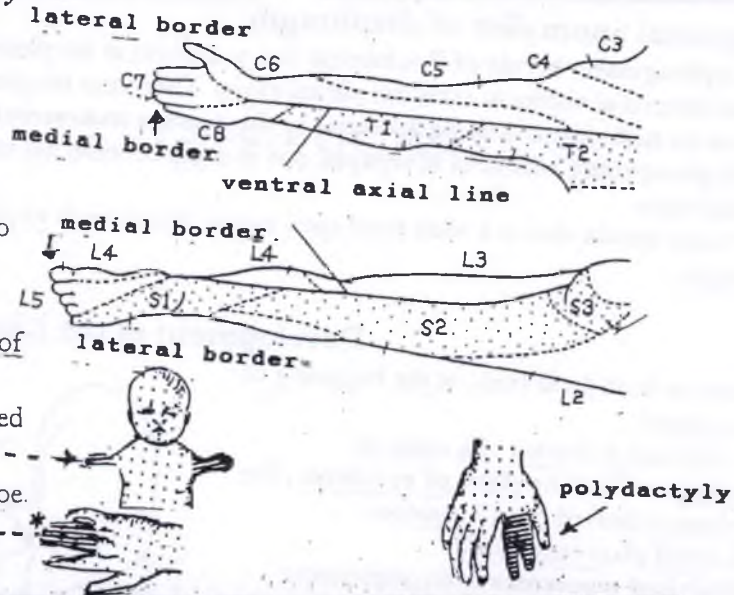
Summary & Illustrations

- The **preaxial** border becomes **medial**.
- The **tibia** (preaxial bone of leg) becomes **medial**.
- Big toe (preaxial digit) becomes **medial**.
- Flexor** surface becomes **posterior**.

In the axis of each limb **chondrification** and then ossification takes place in the mesoderm to form the **bones** of the limbs.

Commonest anomalies

- Amelia**: Complete failure of development of one or more limbs.
- Focomelia**: The hand or the foot is attached directly to the trunk.
- Polydactylia**: Presence of extra finger or toe.
- Syndactyly**: Fusion of two fingers or toes.



DEVELOPMENT OF THE COELOMIC CAVITIES AND SUPRARENAL GLAND

Development of the coelomic cavities

The coelomic cavities (pericardial, pleural and peritoneal cavities) develop from the U-shaped **intra-embryonic coelom** which is formed within the **lateral plate mesoderm**. This is as follows:

- Pericardial cavity**: develops from the **median part** of the U-tube.
- Pleural cavity**: arise from the cranial parts of the 2 limbs of the coelom called **pericardio-peritoneal canals**.
- Peritoneal cavity**: develops from the 2 limbs of the coelom (coelomic ducts).

-The heart tube invaginates the pericardial cavity.

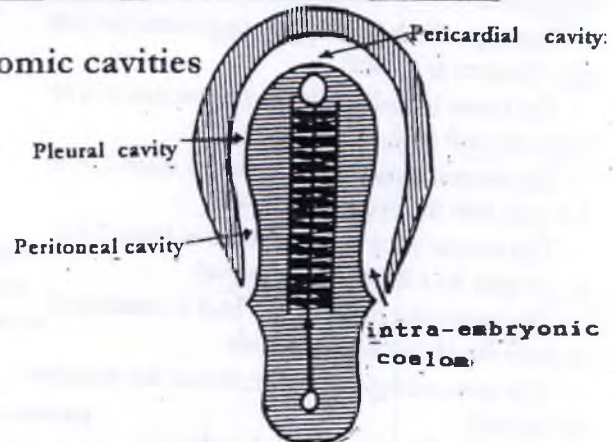
-The lung buds invaginate and expand into the primitive pleural cavities which become shut off the pericardium on one hand and the peritoneal cavity on the other hand as follows:

- Closure of the pleuro-pericardial communication**:

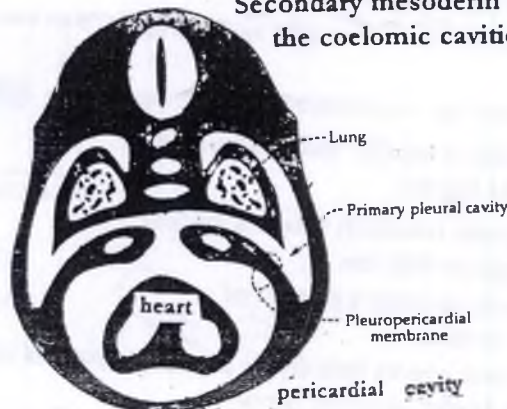
This is produced by a mesodermal septum called the **pleuro-pericardial membrane** (one on each side).

- Closure of the pleuro-peritoneal communication**:

This is produced by the pleuro-peritoneal membrane (one on each side) which forms a part of the diaphragm.



Secondary mesoderm showing the coelomic cavities



Transverse section in the thoracic region of embryo

- The lung buds invaginate the pleural cavities
- The pleuro-pericardial membrane extends to separate the pleura from the pericardial cavity

Summary & Illustrations

Development of the Suprarenal gland

It develops from 2 sources:

1. **Ectodermal origin:** forms its medulla.
2. **Mesodermal origin:** forms its cortex.

Development of the cortex:

– It develops from the **epithelium** (mesothelium) which lines the intraembryonic coelom (mesodermal) **at the angle** between the mesonephros and dorsal mesentery of the gut. The epithelium proliferates to form **fetal cortex**.

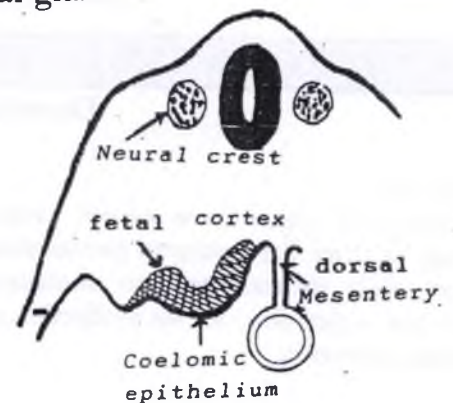
– A second layer of cells develops from the coelomic epithelium and surrounds the fetal cortex forming the **permanent cortex**.

– The **fetal cortex regresses** during the 1st year after birth, being **replaced by the permanent cortex**.

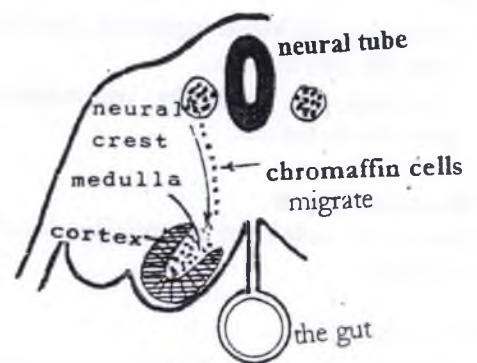
Development of the medulla:

– It is formed by cells from the **neural crest** (ectodermal) which migrate and **invaginate the dorsomedial aspect** of the fetal cortex.

– The majority of its cells are **chromaffin cells** while a few number become **sympathetic cells**.



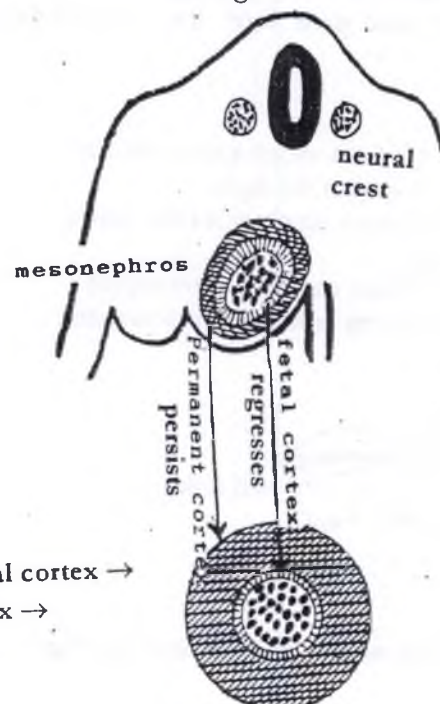
The coelomic epithelium at the angle between mesonephros and dorsal mesentery gives the cortex



Migrating cells from the **neural crest** gives the **medulla**.

Commonest anomalies

1. **Agenesis:** Failure of development of suprarenal gland.
2. **Ectopic suprarenal gland:** Occasionally suprarenal tissue is found between the capsule of the kidney.
3. **Accessory cortical tissue:** may be found on the posterior abdominal wall, and pelvis behind the peritoneum.



The cortex differentiates into **fetal cortex** → **regresses** and **permanent cortex** → proliferates and **persists**.

Summary & Illustrations

DEVELOPMENT OF THE SKIN AND MAMMARY GLAND

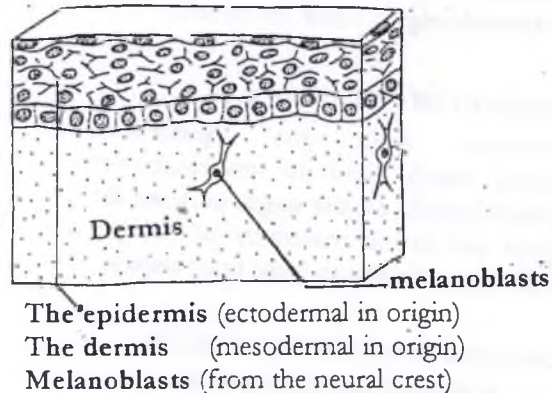
Development of the skin

Epidermis:

Ectodermal in origin. Some **neural crest** cells migrate to enter the epidermis (**melanoblasts**). These cells differentiate into **melanocytes** which are responsible for the production of the **melanin pigments**.

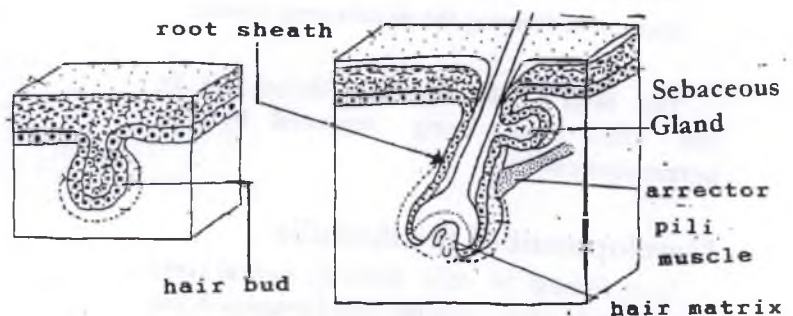
Dermis:

Mesodermal in origin—from **somatopleuric mesoderm** (lateral plate mesoderm) as well as from mesoderm of the **somites**.



Hairs

- develop as epidermal ingrowths (hair buds) to form the root sheaths.
- The deep part forms the hair matrix which gives rise to the hair.

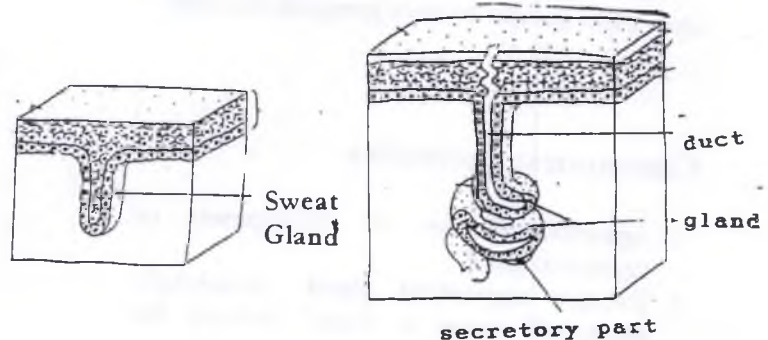


Sebaceous Glands

- arise as side buds from the root sheaths of the hair follicles.

Sweat Glands

- epithelial ingrowths which become canalised.
- Their distal parts are coiled to form the secretory parts.
- Their proximal parts form the ducts of the glands.

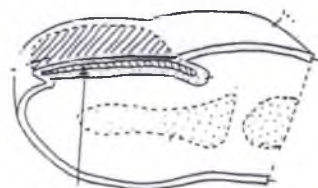


Nails

Appear as a nail fields which are ectodermal thickness on the tip of the digits. They acquire a nerve supply from the ventral (flexor) surface. Later, the nail fields and their nerve supply migrate from the tip onto the dorsal surface of each digit.



A. At first, the nail field at the tip of the digit



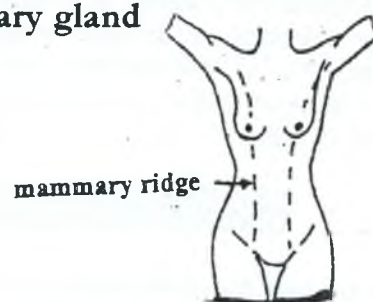
B. Later, the nail field migrates with its nerve supply into the dorsum of the digit.

Summary & Illustrations

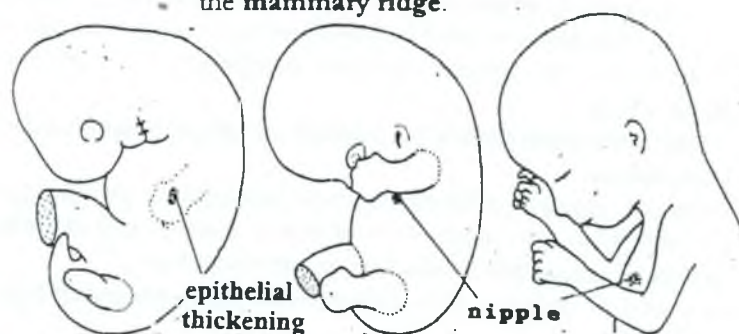
Development of the mammary gland

Mammary ridge (milk-line)

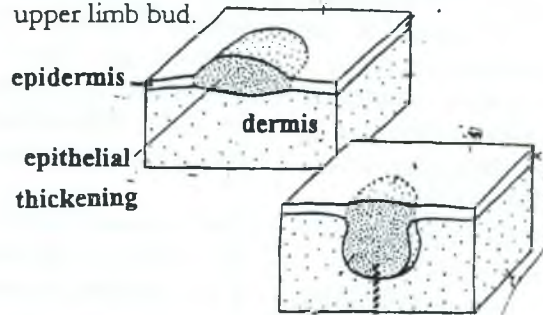
- This is an ectodermal thickening which occurs, on each side, along a line extending from the axilla to the groin.
- In animals several glands develop along this line.
- In man a breast develops on the upper part of the milk ridge (at the level of the developing upper limb).
- Solid ingrowth (**1ry bud**) from the surface ectoderm occur to form the mammary gland.
- The 1ry bud proliferates and gives rise to 15-20 ectodermal **secondary buds** which extend as cords into the underlying mesoderm. These cords become canalized. Their proximal parts form the lactiferous ducts. The distal parts proliferate to form the glands.
- **The underlying mesoderm proliferates to form the stroma of the gland.**
- A depression (**mammary pit**) forms in the epidermis above the gland.
- **The nipple** is formed at full term by proliferation of mesodermal tissue below the pit. This elevates this area above the adjacent skin.
- The lactiferous ducts open into the nipple.
- **At puberty**, the gland enlarges in size by showing new branchings of the lactiferous tubules, in addition to greater deposition of fat between its lobules.



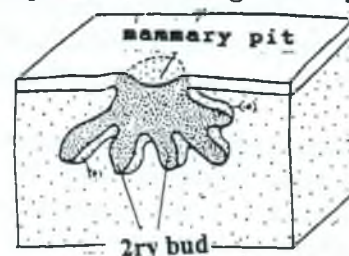
The gland develops on the upper part of the mammary ridge.



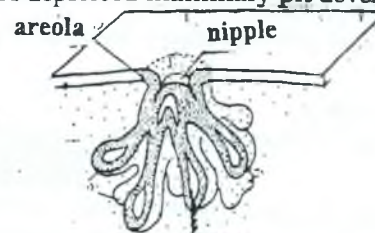
The gland is usually at the level of the upper limb bud.



The epithelial thickening forms **1ry bud**



The 1ry bud branches into **2ry buds**. A depressed **mammary pit** develops.



The 2ry buds give **lactiferous glands, ducts**. The surrounding mesoderm gives **stroma and blood vessels**.

Congenital anomalies:

1. **Amastia**: absence of one or both mammary glands.
2. **Polymastia**: presence of many breasts along the mammary line.
3. **Polythelia**: presence of many nipples along the mammary line.
4. **Micromastia**: abnormally small breasts.
5. **Macromastia**: abnormally large breasts.
6. **Inverted nipple**: due to failure of elevation of the mammary pit.
7. **Gynecomastia**: male developing a female type of breast.



CONGENITAL MALFORMATIONS

A congenital malformation or anomaly is a microscopic or macroscopic defect resulting from defective development. These anomalies are the results of genetic factors, environmental agents, and multifactorial causes. Approximately 3% of neonates have major congenital malformations. A defect may be minor or major, single or in multiples. Most major defects occur in early embryonic development and these embryos usually abort naturally.

Causes of congenital malformations

Genetic factors

Genetic factors are the most important known causes of congenital malformations. Chromosomes may be altered structurally when affected by environmental factors.

If a chromosome breaks, there may be several outcomes: a piece of chromosome may be lost (**deletion**); a piece of chromosome may be transferred to a non-homologous chromosome (**translocation**); a piece of chromosome may become reversed (**inversion**); or a portion of a chromosome may be duplicated (**duplication**).

If the centromere divides transversely instead of longitudinally (**isochromosome**), this can also result in abnormalities.

Abnormal numbers of chromosomes (**aneuploidy**) may also be associated with congenital abnormalities. The condition can result from defective chromosome or chromatid separation (non-disjunction) during the first or second meiotic division in gametogenesis.

Loss of one member of a chromosome pair (**monosomy**) appears to be lethal in human if it affects an autosome.

Gain of a chromosome gives trisomy. **Down's syndrome** is referred to as trisomy 21, which denotes three number 21 chromosomes. Trisomy 13 and 18 are less common. The occurrence of autosomal trisomies increases with maternal age. There are many known abnormalities of the sex chromosome. **Turner's syndrome** is characterized by the presence of only one sex chromosome (XO). Trisomy of sex chromosomes can result in XXY (**Klinefelter's syndrome**), XYY or XXX individuals. Combinations involving four or five X chromosomes have been reported.

Mutant Genes

Malformations can be caused by mutant genes. These are genes which have undergone a change or a loss in function. Often this is a result of environmental factors such as ionising radiation or carcinogenic (cancer inducing) agents. To be inherited, mutations must be present in the germ line.

Environmental agents

Environmental teratogens include drugs, chemicals, infectious agents, radiation and mechanical factors.

Examples of drugs include alcohol, thalidomide, tetracyclines and most anticoagulants.

Chemicals which disturb normal embryogenesis include excess retinoic acid (vitamin A), iodides, and mercury.

Drugs and chemicals together are responsible for less than 2% of recorded congenital malformations.

Infectious agents known to cross the placenta include the rubella virus (German measles), varicella zoster virus (chickenpox) and cytomegalovirus.

Ionizing radiation in large doses has been shown to produce congenital malformations.

Mechanical factors can contribute to postural defects. For example, a significant lack of amniotic fluid (oligohydramnios) can lead to foot deformities.

Multifactorial causes

Most congenital malformations are due to a combination of a genetic predisposition and environmental factors.

Unknown causes

More than half of congenital malformations have no known cause.

Periods of sensitivity

In the course of development, there are periods of sensitivity for each tissue, organ, or system. During these times, the tissue is at its most vulnerable to the actions of teratogens, which are agents that bring about congenital defects. In the first 2 weeks of development, teratogens usually cause embryonic death. During the embryonic period (15-60 days) they may cause major congenital defects, and during the fetal period they may result in structural and functional anomalies.

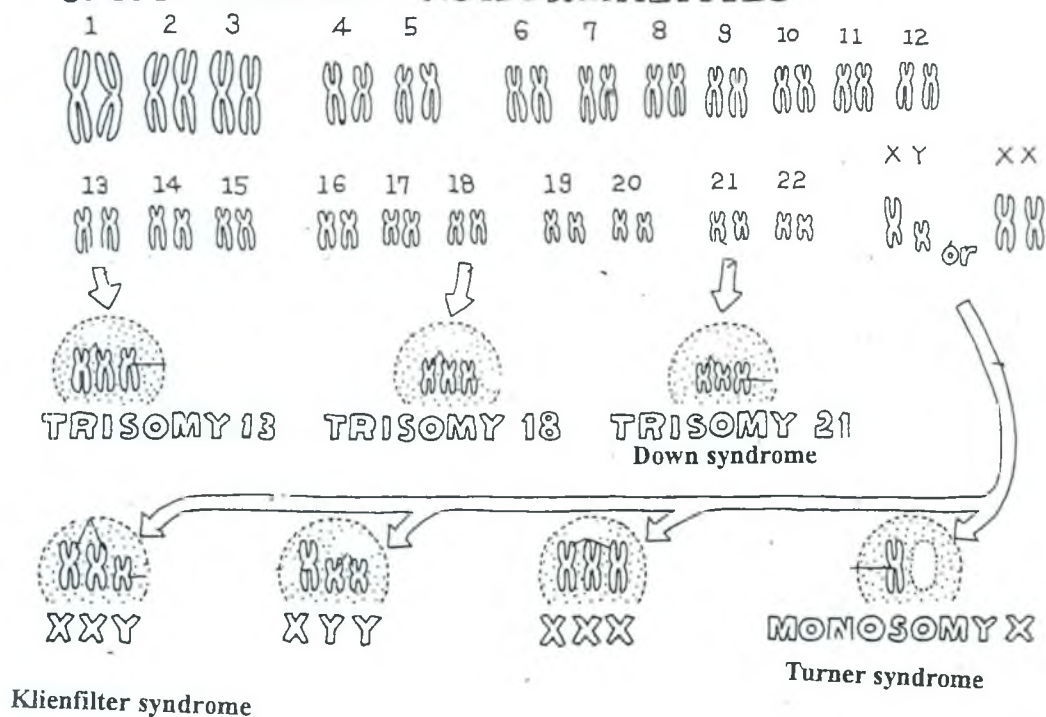
Summary & Illustrations

CONGENITAL MALFORMATIONS

Causes of congenital malformations

▷ GENETIC FACTORS : 15 %

• CHROMOSOMAL ABNORMALITIES



• MUTANT GENES

➔ INHERITED MALFORMATION

▷ ENVIRONMENTAL AGENTS : 10 %

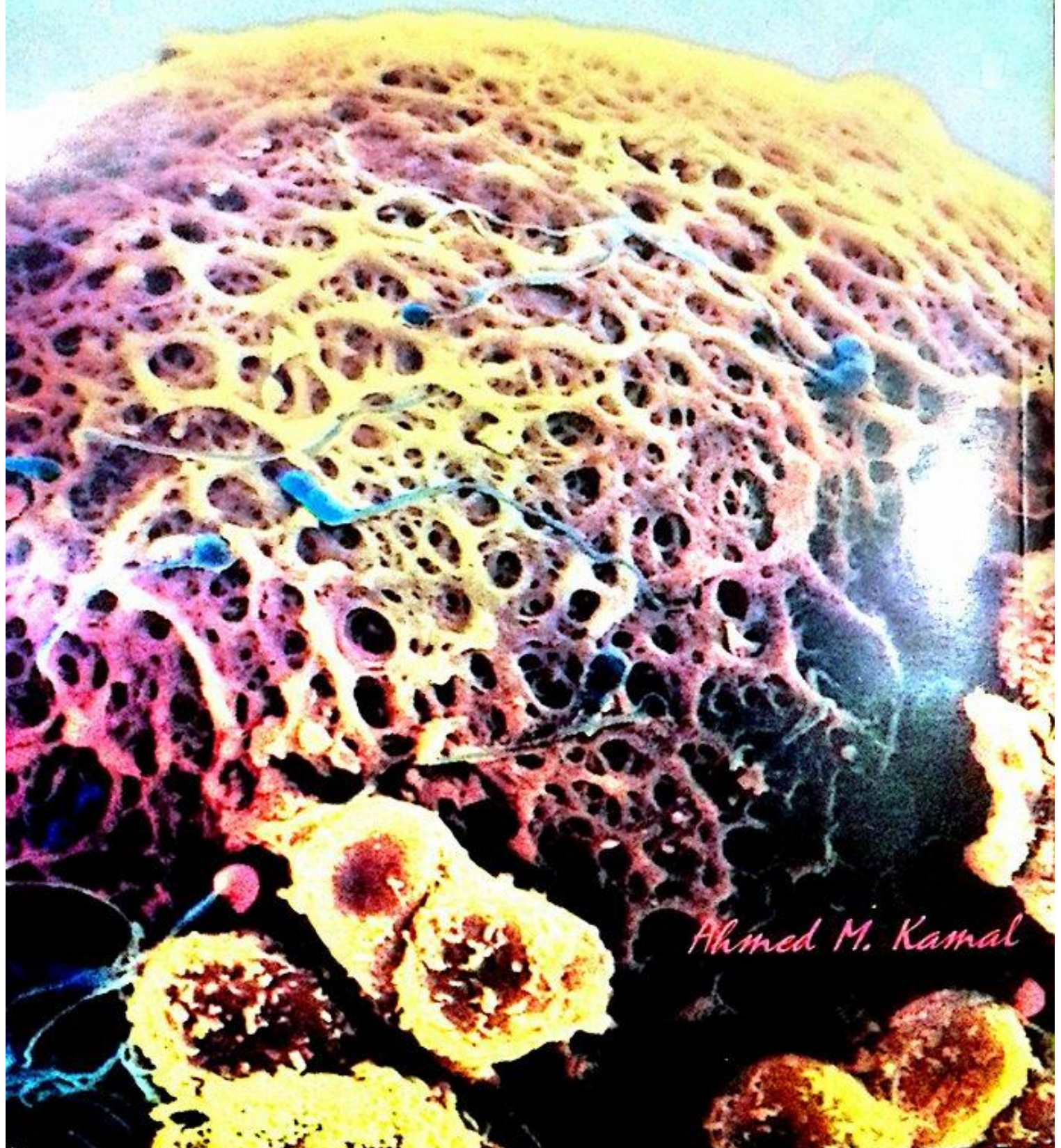


▷ MULTIFACTORIAL CAUSES : 25 %

▷ UNKNOWN CAUSES : > 50 %

Special Embryology

With Summary & Illustrations



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